

**IN THE UNITED STATES DISTRICT COURT FOR THE  
DISTRICT OF MASSACHUSETTS**

<b>PETER J. MILLER, CLIFFORD HOYT, and CAMBRIDGE RESEARCH AND INSTRUMENTATION, INC.,</b>  <b>Plaintiffs,</b>  <b>v.</b>  <b>PATRICK TREADO and CHEMIMAGE CORP.,</b>  <b>Defendants</b>	<b>CIVIL ACTION NO. 05 10367 RWZ</b>
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**DECLARATION OF ANTHONY J. FITZPATRICK, ESQUIRE, IN SUPPORT OF  
DEFENDANTS' MOTION FOR SUMMARY JUDGMENT**

I, Anthony J. Fitzpatrick, Esquire, on my oath swear and depose as follows:

1. I am an attorney admitted to practice in the Commonwealth of Massachusetts and before this Court, and I am a partner in the law firm of Duane Morris LLP, counsel for Defendants ChemImage Corporation and Patrick Treado (collectively, "Defendants").
2. I am make this declaration in support of Defendants' Motion for Summary Judgment.
3. **Exhibit A**, attached hereto, is a true and correct copy of U.S. Patent No. 6,734,962 (hereinafter, "the '962 patent").
4. **Exhibit B**, attached hereto, is a true and correct copy of the April 11, 2005, Preliminary Amendment submitted to the United States Patent and Trademark Office (hereinafter, "PTO") during the reexamination of the '962 patent.

5. **Exhibit C**, attached hereto, is a true and correct copy of the September 25, 2006, Official Action issued by the PTO during the reexamination of the '962 patent.

6. **Exhibit D**, attached hereto, is a true and correct copy of October 16, 2006, Amendment submitted to the PTO in response to the September 25, 2006, Official Action issued by the PTO during the reexamination of the '962 patent.

7. **Exhibit E**, attached hereto, is a true and correct copy of March 17, 2007, Notice of Allowability issued by the PTO during the reexamination of the '962 patent.

8. **Exhibit F**, attached hereto, is a true and correct copy of the Small Business Innovation Research (SBIR) Phase II Report, CI-2570.

9. **Exhibit G**, attached hereto, is a true and correct copy of the March 20, 2007, letter from Teodor J. Holmberg to Judge Rya W. Zobel.

10. **Exhibit H**, attached hereto, is a true and correct copy of the Declaration of Edward S. Yeung.

Signed and sworn under the pains and penalties of perjury this 15th day of June, 2007.

/s/ Anthony J. Fitzpatrick  
Anthony J. Fitzpatrick

(12) **United States Patent**  
**Treado et al.**

(10) **Patent No.:** **US 6,734,962 B2**  
(45) **Date of Patent:** **May 11, 2004**

(54) **NEAR INFRARED CHEMICAL IMAGING MICROSCOPE**

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**Matthew Nelson**, Pittsburgh, PA (US);  
**Scott Keitzer**, Export, PA (US)

(73) Assignee: **ChemImage Corporation**, Pittsburgh, PA (US)

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 201 days.

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(22) Filed: **Oct. 12, 2001**

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**Related U.S. Application Data**

(60) Provisional application No. 60/239,969, filed on Oct. 13, 2000.

(51) **Int. Cl.<sup>7</sup>** ..... **G01J 3/44**

(52) **U.S. Cl.** ..... **356/301; 356/51; 356/326; 356/331; 250/339.05**

(58) **Field of Search** ..... 356/301, 51, 310, 356/326, 328, 330–334, 73; 250/339.05, 339.02, 339.01, 339.07, 339, 458.1, 459.1, 461.1, 462.2; 382/284

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*Assistant Examiner*—Layla Lauchman

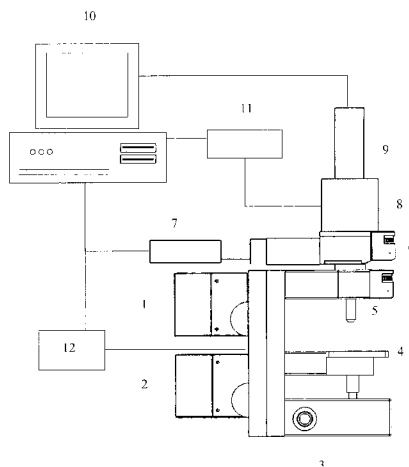
(74) *Attorney, Agent, or Firm*—Buchanan Ingersoll, P.C.

(57)

**ABSTRACT**

A chemical imaging system is provided which uses a near infrared radiation microscope. The system includes an illumination source which illuminates an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength. A multitude of spatially resolved spectra of transmitted, reflected, emitted or scattered near infrared wavelength radiation light from the illuminated area of the sample is collected and a collimated beam is produced therefrom. A near infrared imaging spectrometer is provided for selecting a near infrared radiation image of the collimated beam. The filtered images are collected by a detector for further processing. The visible wavelength light from the illuminated area of the sample is simultaneously detected providing for the simultaneous visible and near infrared chemical imaging analysis of the sample. Two efficient means for performing three dimensional near infrared chemical imaging microscopy are provided.

**16 Claims, 6 Drawing Sheets**



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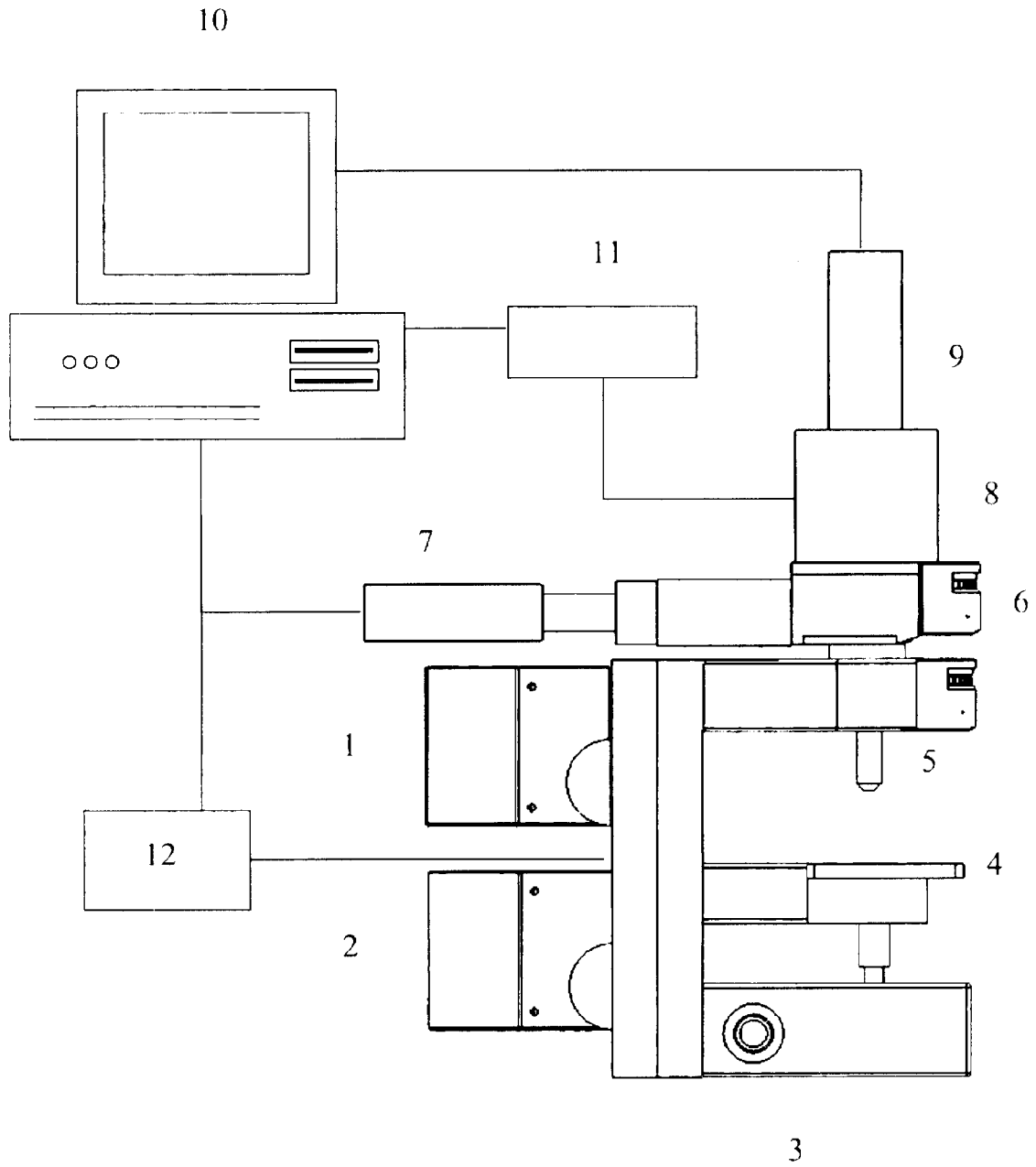


Figure 1

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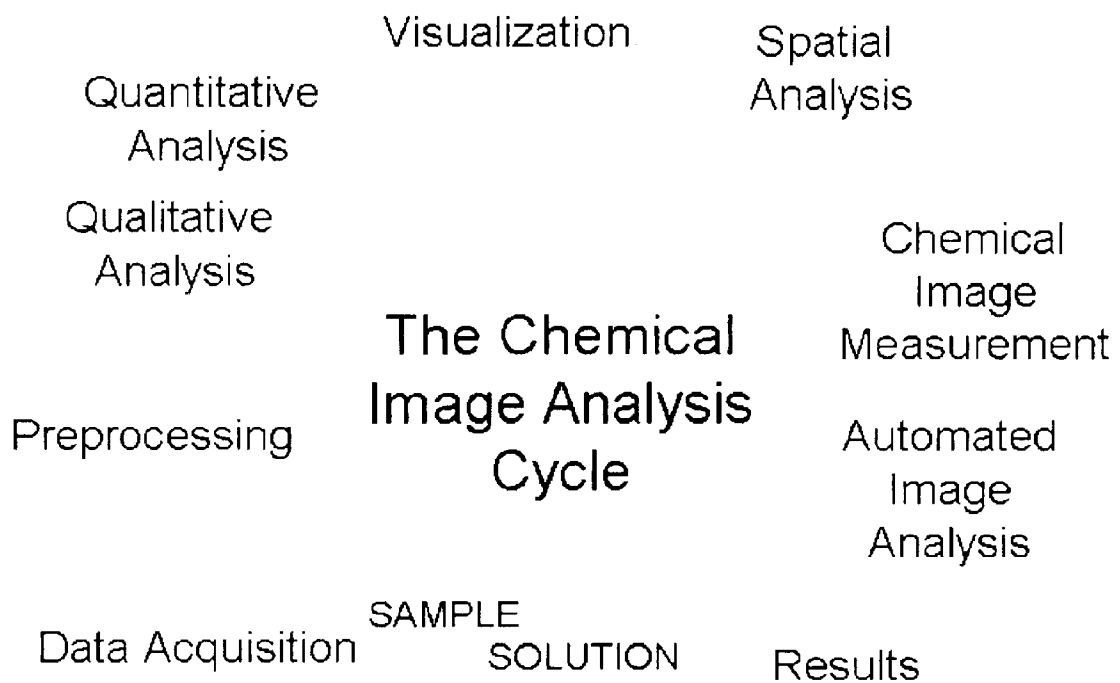


Figure 2

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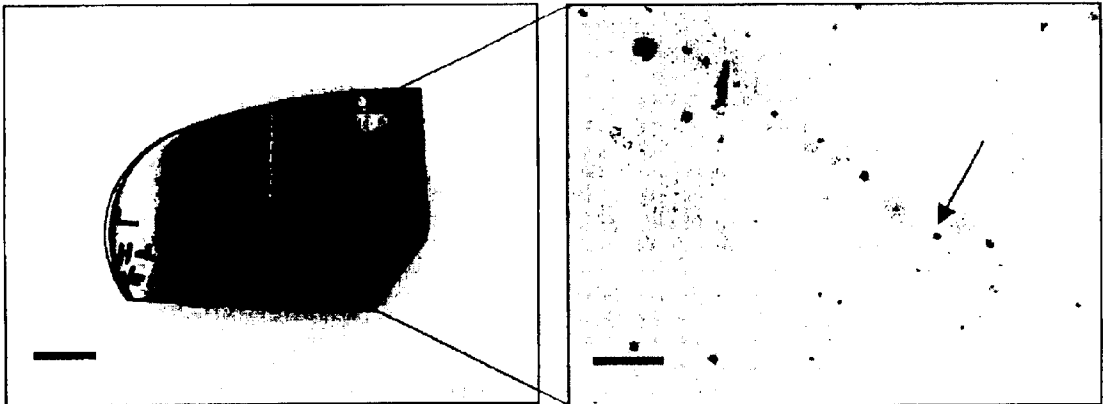


Figure 3

Figure 4

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Figure 5A

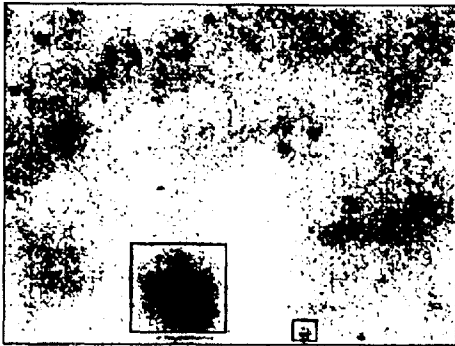


Figure 5B

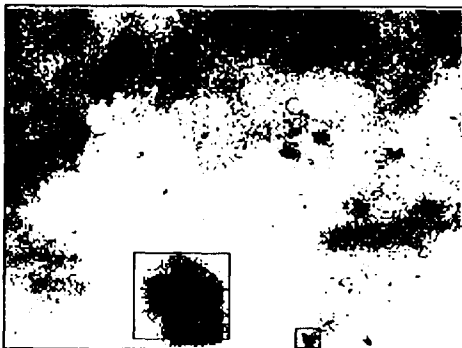
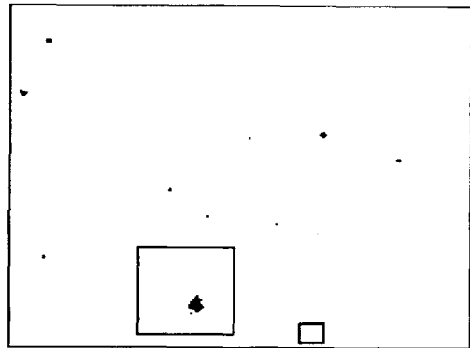


Figure 5C

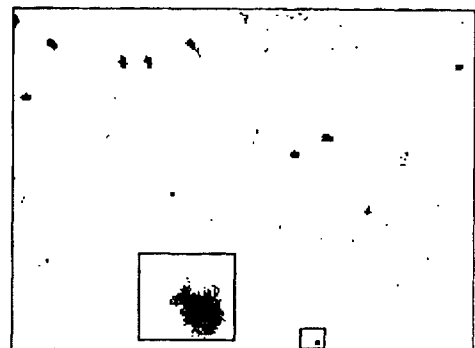


Figure 5D

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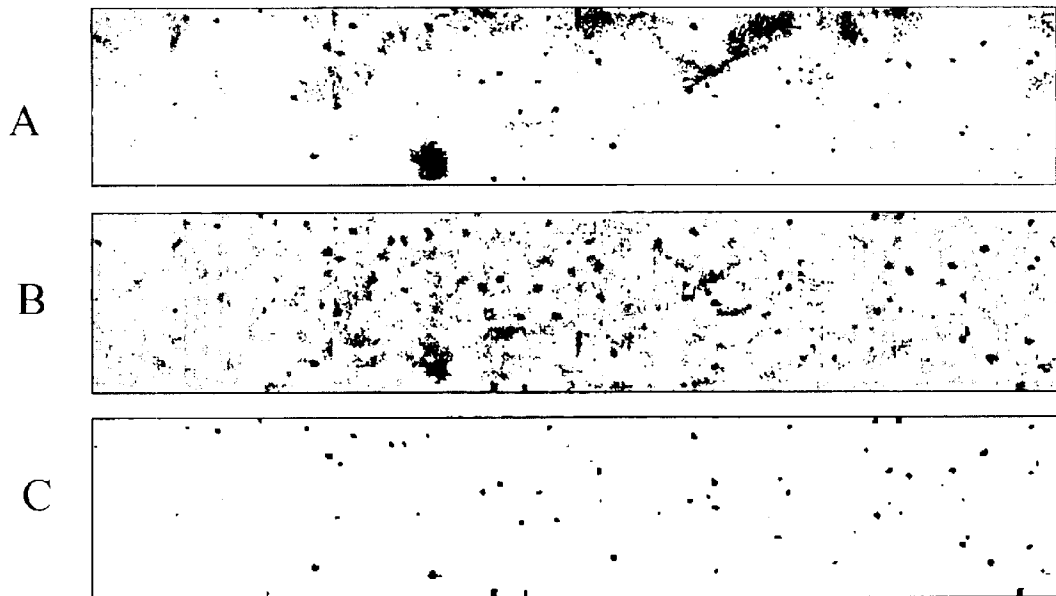


Figure 6

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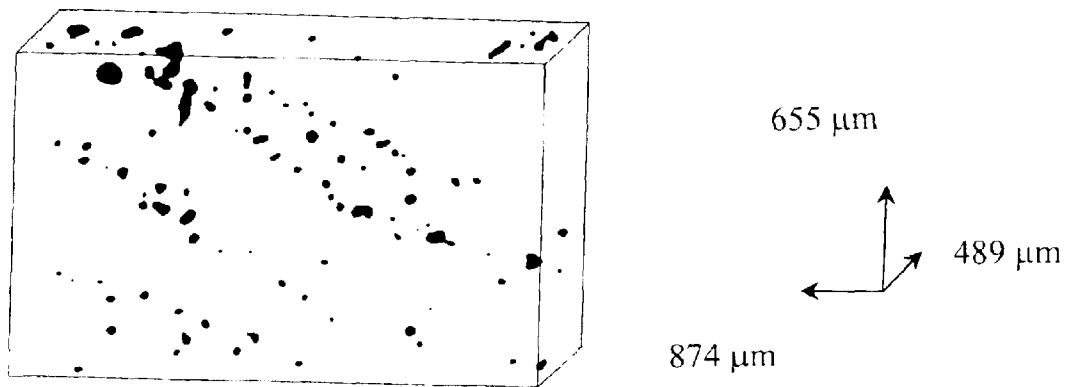


Figure 7

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## NEAR INFRARED CHEMICAL IMAGING MICROSCOPE

This application claims the benefit of U.S. Provisional Application No. 60/239,969, entitled "Near Infrared Chemical Imaging Microscope" filed Oct. 13, 2000.

This work is supported by the National Institute of Standards and Technology (NIST) under the Advanced Technology Program (ATP) award (Contract Number 70NANB8H4021)

### FIELD OF INVENTION

The present invention is related to near-infrared (NIR) microscopes for spectroscopic and image analysis, and, in particular, to microscopes useful for both NIR spectroscopy, NIR chemical imaging and NIR volumetric chemical imaging.

### BACKGROUND OF THE INVENTION

NIR spectroscopy is a mature, non-contact, non-destructive analytical characterization tool that has been widely applied to a broad range of materials. The NIR region of the electromagnetic spectrum encompasses radiation with wavelengths of 0.78 to 2.5  $\mu\text{m}$  (12,800 to 4,000  $\text{cm}^{-1}$ ). NIR spectra result from the overtone and combination bands of fundamental mid-infrared (MIR) bands. Among the many desirable characteristics, NIR is used to rapidly obtain both qualitative and quantitative information about the molecular makeup of a material. Digital imaging, on the other hand, provides a means to obtain optical (i.e., spatial—morphological, topographical, etc.) information about a material. By combining the spatial information obtained from digital imagery and the spectral information obtained from NIR spectroscopy, the chemical makeup of complex material matrices can be mapped out in both two and three spatial dimensions. NIR chemical imaging combines NIR spectroscopy and digital imaging for the molecular-specific analysis of materials. A NIR chemical imaging microscope apparatus employing NIR absorption molecular spectroscopy for materials characterization is disclosed.

State-of-the-Art Instrumentation

NIR microscopes are used to obtain NIR absorption, transmittance or reflectance spectra (e.g., NIR microspectra) from samples ranging in size between 1 and 1000  $\mu\text{m}$ . These instruments are typically equipped with a digital camera to visually locate a region of interest on a sample upon which a NIR light beam from a Fourier transform (FT) spectrometer is focused. Reflective optics are used to direct the transmitted or reflected light from the sample to a NIR detector. The output is a NIR absorption spectrum collected in transmittance or reflectance mode.

NIR chemical imaging can be considered an extension of NIR microspectroscopy. Much of the imaging performed since the development of the first NIR microprobes has involved spatial scanning of samples beneath NIR microscopes in order to construct NIR "maps" of surfaces. In point by point scanning with NIR microscopes, the NIR light beam is focused onto the surface of a sample or apertured to illuminate a small region of a sample and a spectrum from each spatial position is collected. Images are obtained by rastering the sample through the focused or apertured NIR light beam and the spectra recorded are then reconstructed to form an image. Although point scanning produces images based on NIR contrast, long experimental times are common since the duration of the experiment is proportional to the number of image pixels. As a direct result, point scan images

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are captured at low image definition, which relates directly to the limited utility of the technique as an imaging tool for the routine assessment of material morphology. The spatial resolution of the image is limited by the size of the NIR illumination spot on the sample (no less than 1  $\mu\text{m}$ ) and the rastering mechanism, which requires the use of moving mechanical parts that are challenging to operate reproducibly.

NIR imaging cameras have been used in photography for decades. Until recently, however, it has not been easily accessible to those not versed in traditional photographic processes. By using optical filters (e.g., cold filters) that block the visible wavelengths (0.4–0.78  $\mu\text{m}$ ), charge-coupled devices (CCDs) used in digital cameras and camcorders can be used to sense NIR light out to around 1100 nm. Other regions of the NIR spectrum can be viewed using devices such as indium gallium arsenide (InGaAs—0.9  $\mu\text{m}$  to 1.7  $\mu\text{m}$ ) and indium antimonide (InSb—1.0  $\mu\text{m}$  to 5.0  $\mu\text{m}$ ) focal plane array (FPA) detectors. These integrated wavelength NIR imaging approaches allow one to study relative light intensities of objects over broad ranges of the NIR spectrum, but useful chemical information is unattainable without the use of some type of discrete wavelength filtering device.

The use of dielectric interference filters in combination with NIR FPAs is one method in which chemical information can be obtained from a sample. To form NIR chemical images, a NIR light beam is defocused to illuminate a wide field of view and the reflected or transmitted light from the illuminated area is imaged onto a two-dimensional NIR detector. A selection of discrete dielectric interference filters provided in a filter wheel, or a linearly variable or circularly variable format can be positioned in front of a broadband NIR light source, or in front of the NIR FPA itself in order to collect NIR wavelength resolved images. Typically, the use of several fixed bandpass filters is required to access the entire NIR spectrum. The spatial resolution of the NIR image approaches that of the optical microscope, while spectral resolution of several nanometers has been demonstrated. Key limitations of the dielectric filter approach include the need for a multitude of discrete filters to provide appreciable free spectral range, or the reliance on moving mechanical parts in employing continuously tunable dielectric interference filters as a requirement to form wavelength resolved images. While moving mechanical assemblies can be engineered they add cost and complexity to NIR chemical imaging systems. Alternatives to moving mechanical assemblies are generally more cost effective and provide performance advantages.

Acousto-optic tunable filters (AOTFs) have been employed as no-moving-parts imaging spectrometers for NIR imaging. The AOTF is a solid-state device that is capable of functioning from the UV to the mid-IR depending on the choice of the filter's crystal material. Operation of the AOTF is based on the interaction of light with a traveling acoustic sound wave in an anisotropic crystal medium. The incident light is diffracted with a narrow spectral bandpass when an rf signal is applied to the device. By changing the applied rf frequency under computer control the spectral passband can be tuned rapidly with the benefit of non-moving parts.

For use in NIR chemical imaging, AOTFs have distinct limitations. AOTFs have imaging performance that is degraded appreciably from diffraction-limited conditions due to dispersion effects and image shifting effects. Furthermore, AOTFs suffer from temperature instability and exhibit nonlinear properties that complicate their use as imaging spectrometers.

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An aim of NIR chemical imaging technology development has been to develop a NIR imaging technique that combines diffraction-limited spatial resolution with high spectral resolution. NIR chemical imaging techniques have only recently achieved a degree of technological maturity that allow the collection of high resolution (spectral and spatial) data with the advent of the liquid crystal (LC) imaging spectrometers. In general, LC devices provide diffraction-limited spatial resolution. The spectral resolution of the LC imaging spectrometer is comparable to that provided by dispersive monochromator and Fourier transform interferometers. In addition, LC technology provides high out of band rejection, broad free spectral range, moderate transmittance, high overall etendue and highly reproducible random access computer controlled tuning.

Under normal NIR imaging operation, LC imaging spectrometers allow NIR chemical images of samples to be recorded at discrete wavelengths (energies). A spectrum is generated corresponding to thousands of spatial locations at the sample surface by tuning the LC imaging spectrometer over a range of wavelengths and collecting NIR images systematically. Contrast is generated in the images based on the relative amounts of NIR absorption, transmittance or reflectance that is generated by the different species located throughout the sample. Since a high quality NIR spectrum is generated for each pixel location, a wide variety of chemometric analysis tools, both univariate and multivariate, can be applied to the NIR image data to extract pertinent information. Correlative multivariate routines are particularly powerful when applied to chemical images collected from samples intentionally seeded with a known standard material. This approach of incorporating calibration standards within an image field of view can be extended to quantitative chemical image analysis. In addition, digital image analysis procedures can also be applied to high image quality NIR chemical images to perform routine particle analysis in both two (2D) and three (3D) spatial dimensions. Volumetric 3D NIR chemical image analysis can be performed very effectively using numerical deconvolution computational strategies.

#### SUMMARY OF THE INVENTION

To address the need for a device that can provide video imaging, NIR spectroscopy and high resolution (spatial and spectral) NIR chemical imaging in two and three spatial dimensions, a novel NIR chemical imaging microscope has been developed that is NIR chemical imaging capable.

The microscope design uses NIR optimized liquid crystal (LC) imaging spectrometer technology for wavelength selection. The NIR optimized refractive microscope is used in conjunction with infinity-corrected objectives to form the NIR image on the detector with or without the use of a tube lens. An integrated parfocal analog color CCD detector provides real-time sample positioning and focusing. The color image and the NIR image are fused in software. In one configuration, the NIR microscope may be used as a volumetric imaging instrument through the means of moving the sample through focus, collecting images at varying focal depths and reconstructing a volumetric image of the sample in software, or through the means of keeping the sample fixed and changing the wavelength dependent depth of penetration in conjunction with a refractive tube lens with a well characterized chromatic effect. The output of the microscope can be coupled to a NIR spectrometer either via direct optical coupling or via a fiber optic. A Chemical Imaging Addition Method seeds the sample with a material of known composition, structure and/or concentration and then gen-

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erates the NIR image suitable for qualitative and quantitative analysis. The microscope generates NIR chemical image data that is analyzed and visualized using chemical image analysis software in a systematic and comprehensive manner. While this invention has been demonstrated on a microscope optic platform, the novel concepts are also applicable to other image gathering platforms, namely fiberscopes, macrolens systems and telescopes.

#### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a schematic diagram of the near-infrared (NIR) chemical imaging microscope

FIG. 2 shows a diagram of the chemical imaging data analysis cycle performed in software.

FIG. 3 is a digital brightfield image of a CdZnTe semiconductor material decorated with tellurium inclusions.

FIG. 4 an NIR microscopic transmittance image of a CdZnTe semiconductor material decorated with tellurium inclusions.

FIG. 5A illustrates a raw NIR image frame of a CdZnTe wafer sample.

FIG. 5B illustrates an NIR image frame of the sample of FIG. 5A in which the threshold value for the image was set too low.

FIG. 5C illustrates an NIR image frame of the sample of FIG. 5A in which the threshold value for the image was set too high.

FIG. 5D illustrates an NIR image frame of the sample of FIG. 5A in which the threshold value for the image was set to an intermediate level.

FIG. 6A is the original raw image of four adjacent regions of interest on a CdZnTe wafer.

FIG. 6B is the background-corrected image corresponding to the four adjacent regions of interest of the CdZnTe wafer of FIG. 6A.

FIG. 6C is the binarized image corresponding to the four adjacent regions of interest of the CdZnTe wafer of FIG. 6A.

FIG. 7 is a three-dimensional view of tellurium inclusions in a CdZnTe wafer.

#### DETAILED DESCRIPTION OF THE INVENTION

The NIR chemical imaging microscope combines in a single platform a NIR optimized refractive optical microscope base, which is equipped with NIR optimized infinity-corrected microscope objectives, an automated XYZ translational microscope stage and quartz tungsten halogen (QTH) lamps to secure and illuminate samples for NIR spectroscopy and imaging, an analog color charge-coupled device (CCD) detector for ordinary optical image collection and digital image collection, a NIR LC imaging spectrometer for NIR chemical image wavelength selection and a room temperature or optionally cooled NIR FPA for NIR image capture.

FIG. 1 is a schematic diagram of the NIR chemical imaging microscope. NIR illumination is directed to the sample in a reflected light configuration using a QTH source or other broadband white light source, including metal halide or Xe arc lamps 1 or a transmitted light configuration using QTH or suitable NIR source 2 of an NIR optimized refractive optical microscope platform 3. The reflected or transmitted NIR light is collected from the sample positioned on the automated XYZ translational microscope stage 4 through an infinity-corrected NIR optimized microscope objective 5.

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Ordinary optical imagery of the sample can be obtained using a mirror or beamsplitter or prism arrangement inserted into turret 6 and collecting an image with an analog or digital color or monochrome charge-coupled device (CCD) or CMOS detector 7. In NIR chemical imaging mode, the magnified NIR image is coupled through a NIR LC imaging spectrometer 8 and collected on a room temperature or cooled NIR focal plane array (FPA) detector 9. The FPA is typically comprised of indium gallium arsenide (InGaAs), but may be comprised of other NIR sensitive materials, including platinum silicide (PtSi), indium antimonide (InSb) or mercury cadmium telluride (HgCdTe). Using a beam-splitting element inserted into turret 6, NIR and ordinary optical imagery can be collected with an analog monochrome or color CCD detector 7 and NIR FPA 9 simultaneously.

A central processing unit 10, typically a Pentium computer, is used for NIR chemical image collection and processing. The analog color CCD 7, NIR FPA 9, automated XYZ translational microscope stage 4 controlled via a controller 12 and NIR LC imaging spectrometer 8 (through LC imaging spectrometer controller 11) are operated with commercial software, such as Acquisition Manager (Chemlcon Inc.) in conjunction with ChemImage (Chemlcon Inc.).

By introducing a polarization sensitive beam splitting element in the optical path prior to the NIR LC imaging spectrometer 8 (not shown in schematic diagram), a portion of the NIR light from the sample may be coupled to a remote NIR spectrometer (also not shown in schematic diagram).

Preferably, NIR optimized liquid crystal (LC) imaging spectrometer technology is used for wavelength selection. The LC imaging spectrometer may be of the following types: Lyot liquid crystal tunable filter (LCTF); Evans Split-Element LCTF; Solc LCTF; Ferroelectric LCTF; Liquid crystal Fabry Perot (LCFP); or a hybrid filter technology comprised of a combination of the above-mentioned LC filter types or the above mentioned filter types in combination with fixed bandpass and bandreject filters comprised of dielectric, rugate, holographic, color absorption, acousto-optic or polarization types.

One novel component of this invention, is that a NIR optimized refractive microscope is used in conjunction with infinity-corrected objectives to form the NIR image on the detector without the use of a tube lens. The microscope can be optimized for NIR operation through inherent design of objective and associated anti-reflective coatings, condenser and light source. To simultaneously provide high numerical apertures the objective should be refractive. To minimize chromatic aberration, maximize throughput and reduce cost the conventional tube lens can be eliminated, while having the NIR objective form the NIR image directly onto the NIR focal plane array (FPA) detector, typically of the InGaAs type. The FPA can also be comprised of Si, SiGe, PtSi, InSb, HgCdTe, PdSi, Ge, analog vidicon types. The FPA output is digitized using an analog or digital frame grabber approach.

An integrated parfocal analog CCD detector provides real-time sample positioning and focusing. An analog video camera sensitive to visible radiation, typically a color or monochrome CCD detector, but may be comprised of a CMOS type, is positioned parfocal with the NIR FPA detector to facilitate sample positioning and focusing without requiring direct viewing of the sample through conventional eyepieces. The video camera output is typically digitized using a frame grabber approach.

The color image and the NIR image are fused using software. While the NIR and visible cameras often generate

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images having differing contrast, the sample fields of view can be matched through a combination of optical and software manipulations. As a result, the NIR and visible images can be compared and even fused through the use of overlay techniques and correlation techniques to provide the user a near-real time view of both detector outputs on the same computer display. The comparative and integrated views of the sample can significantly enhance the understanding of sample morphology and architecture. By comparing the visible, NIR and NIR chemical images, additional useful information can be acquired about the chemical composition, structure and concentration of species in samples.

The NIR microscope can be used as a volumetric imaging instrument through the means of moving the sample through focus in the Z, axial dimension, collecting images in and out of focus and reconstructing a volumetric image of the sample in software. For samples having some volume (bulk materials, surfaces, interfaces, interphases), volumetric chemical imaging in the NIR has been shown to be useful for failure analysis, product development and routine quality monitoring. The potential also exists for performing quantitative analysis simultaneous with volumetric analysis. Volumetric imaging can be performed in a non-contact mode without modifying the sample through the use of numerical confocal techniques, which require that the sample be imaged at discrete focal planes. The resulting images are processed and reconstructed and visualized. Computational optical sectioning reconstruction techniques based on a variety of strategies have been demonstrated, including nearest neighbors and iterative deconvolution.

An alternative to sample positioning combined with computation reconstruction is to employ a tube lens in the image formation path of the microscope which introduces chromatic aberration. As a result the sample can be interrogated as a function of sample depth by exercising the LC imaging spectrometer, collecting images at different wavelengths which penetrate to differing degrees into bulk materials. These wavelength dependent, depth dependent images can be reconstructed to form volumetric images of materials without requiring the sample to be moved, again through application of computational optical sectioning reconstruction algorithms.

The output of the microscope can be coupled to a NIR spectrometer either via direct optical coupling or via a fiber optic cable. This allows conventional spectroscopic tools to be used to gather NIR spectra for traditional, high speed spectral analysis. The spectrometers can be of the following types: fixed filter spectrometers; grating based spectrometers; Fourier Transform spectrometers; or Acousto-Optic spectrometers.

A novel method that is readily employed by the disclosed microscope invention is a method described as the Chemical Imaging Addition Method which involves seeding the sample with a material of known composition, structure and/or concentration and then generating the NIR image suitable for qualitative and quantitative analysis. The Chemical Imaging Addition Method is a novel extension of a standard analytical chemical analysis technique, the Standard Addition Method. A common practice in quantitative chemical analysis is to construct a standard calibration curve which is a plot of analytical response for a particular technique as a function of known analyte concentration. By measuring the analytical response from an unknown sample, an estimate of the analyte concentration can then be extrapolated from the calibration curve. In the Standard Addition Method, known quantities of the analyte are added to the

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samples and the increase in analytical response is measured. When the analytical response is linearly related to concentration, the concentration of the unknown analyte can be found by plotting the analytical response from a series of standards and extrapolating the unknown concentration from the curve. In this graph, however, the x-axis is the concentration of added analyte after being mixed with the sample. The x-intercept of the curve is the concentration of the unknown following dilution. The primary advantage of the standard addition method is that the matrix remains constant for all samples.

While the Standard Addition Method is used specifically for quantitative analysis, the Chemical Imaging Addition Method can be used for qualitative and quantitative analysis. The Chemical Imaging Addition Method relies upon spatially isolating analyte standards in order to calibrate the Chemical Imaging analysis. In chemical imaging, thousands of linearly independent, spatially-resolved spectra are collected in parallel of analytes found within complex host matrices. These spectra can then be processed to generate unique contrast intrinsic to analyte species without the use of stains, dyes, or contrast agents. Various spectroscopic methods including near-infrared (NIR) absorption spectroscopy can be used to probe molecular composition and structure without being destructive to the sample. Similarly, in NIR chemical imaging the contrast that is generated reveals the spatial distribution of properties revealed in the underlying NIR spectra.

The Chemical Imaging Addition Method can involve several data processing steps, typically including, but not limited to:

1. Ratiometric correction in which the sample NIR image is divided by the background NIR image to produce a result having a floating point data type.
2. The divided image is normalized by dividing each intensity value at every pixel in the image by the vector norm for its corresponding pixel spectrum. Where the vector norm is the square root of the sum of the squares of pixel intensity values for each pixel spectrum. Normalization is applied for qualitative analysis of NIR chemical images. For quantitative analysis, normalization is not employed, but relies instead on the use of partial least squares regression (PLSR) techniques.
3. Correlation analysis, including Euclidian Distance and Cosine correlation analysis (CCA) are established multivariate image analysis techniques that assess similarity in spectral image data while simultaneously suppressing background effects. More specifically, CCA assesses chemical heterogeneity without the need for training sets, identifies differences in spectral shape and efficiently provides chemical image based contrast that is independent of absolute intensity. The CCA algorithm treats each pixel spectrum as a projected vector in n-dimensional space, where n is the number of wavelengths sampled in the image. An orthonormal basis set of vectors is chosen as the set of reference vectors and the cosine of the angles between each pixel spectrum vector and the reference vectors are calculated. The intensity values displayed in the resulting CCA images are these cosine values, where a cosine value of 1 indicates the pixel spectrum and reference spectrum are identical, and a cosine value of 0 indicates the pixel spectrum and the reference spectrum are orthogonal (no correlation). The dimensions of the resulting CCA image is the same as the original image because the orthonormal basis set provides n reference vectors, resulting in n CCA images.

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4. Principal component analysis (PCA) is a data space dimensionality reduction technique. A least squares fit is drawn through the maximum variance in the n-dimensional dataset. The vector resulting from this least squares fit is termed the first principal component (PC) or the first loading. After subtracting the variance explained from the first PC, the operation is repeated and the second principal component is calculated. This process is repeated until some percentage of the total variance in the data space is explained (normally 95% or greater). PC Score images can then be visualized to reveal orthogonal information including sample information, as well as instrument response, including noise. Reconstruction of spectral dimension data can then be performed guided by cluster analysis, including without PCs that describe material or instrument parameters that one desires to amplify or suppress, depending on the needs of the sensing application.

Effective materials characterization with the disclosed NIR chemical imaging microscope invention typically requires application of a multitude of software procedures to the NIR chemical image. A schematic of the chemical image analysis cycle is shown in FIG. 2. A fairly comprehensive description of the variety of steps used to process chemical images is described below.

Until recently, seamless integration of spectral analysis, chemometric analysis and digital image analysis has not been commercially available. Individual communities have independently developed advanced software applicable to their specific requirements. For example, digital imaging software packages that treat single-frame gray-scale images and spectral processing programs that apply chemometric techniques have both reached a relatively mature state. One limitation to the development of chemical imaging, however, has been the lack of integrated software that combines enough of the features of each of these individual disciplines to have practical utility.

Historically, practitioners of chemical imaging were forced to develop their own software routines to perform each of the key steps of the data analysis. Typically, routines were prototyped using packages that supported scripting capability, such as Matlab, IDL, Grams or LabView. These packages, while flexible, are limited by steep learning curves, computational inefficiencies, and the need for individual practitioners to develop their own graphical user interface (GUI). Today, commercially available software does exist that provides efficient data processing and the ease of use of a simple GUI.

Software that meets these goals must address the entirety of the chemical imaging process. The chemical imaging analysis cycle illustrates the steps needed to successfully extract information from chemical images and to tap the full potential provided by chemical imaging systems. The cycle begins with the selection of sample measurement strategies and continues through to the presentation of a measurement solution. The first step is the collection of images. The related software must accommodate the full complement of chemical image acquisition configurations, including support of various spectroscopic techniques, the associated spectrometers and imaging detectors, and the sampling flexibility required by differing sample sizes and collection times. Ideally, even relatively disparate instrument designs can have one intuitive GUI to facilitate ease of use and ease of adoption.

The second step in the analysis cycle is data preprocessing. In general, preprocessing steps attempt to minimize contributions from chemical imaging instrument response

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that are not related to variations in the chemical composition of the imaged sample. Some of the functionalities needed include: correction for detector response, including variations in detector quantum efficiency, bad detector pixels and cosmic events; variation in source illumination intensity across the sample; and gross differentiation between spectral lineshapes based on baseline fitting and subtraction. Examples of tools available for preprocessing include ratio-metric correction of detector pixel response; spectral operations such as Fourier filters and other spectral filters, normalization, mean centering, baseline correction, and smoothing; spatial operations such as cosmic filtering, low-pass filters, high-pass filters, and a number of other spatial filters.

Once instrument response has been suppressed, qualitative processing can be employed. Qualitative chemical image analysis attempts to address a simple question, "What is present and how is it distributed?". Many chemometric tools fall under this category. A partial list includes: correlation techniques such as cosine correlation and Euclidean distance correlation; classification techniques such as principal components analysis, cluster analysis, discriminant analysis, and multi-way analysis; and spectral deconvolution techniques such as SIMPLISMA, linear spectral unmixing and multivariate curve resolution.

Quantitative analysis deals with the development of concentration map images. Just as in quantitative spectral analysis, a number of multivariate chemometric techniques can be used to build the calibration models. In applying quantitative chemical imaging, all of the challenges experienced in non-imaging spectral analysis are present in quantitative chemical imaging, such as the selection of the calibration set and the verification of the model. However, in chemical imaging additional challenges exist, such as variations in sample thickness and the variability of multiple detector elements, to name a few. Depending on the quality of the models developed, the results can range from semi-quantitative concentration maps to rigorous quantitative measurements.

Results obtained from preprocessing, qualitative analysis and quantitative analysis must be visualized. Software tools must provide scaling, automapping, pseudo-color image representation, surface maps, volumetric representation, and multiple modes of presentation such as single image frame views, montage views, and animation of multidimensional chemical images, as well as a variety of digital image analysis algorithms for look up table (LUT) manipulation and contrast enhancement.

Once digital chemical images have been generated, traditional digital image analysis can be applied. For example, Spatial Analysis and Chemical Image Measurement involve binarization of the high bit depth (typically 32 bits/pixel) chemical image using threshold and segmentation strategies. Once binary images have been generated, analysis tools can examine a number of image domain features such as size, location, alignment, shape factors, domain count, domain density, and classification of domains based on any of the selected features. Results of these calculations can be used to develop key quantitative image parameters that can be used to characterize materials.

The final category of tools, Automated Image Processing, involves the automation of key steps or of the entire chemical image analysis process. For example, the detection of well defined features in an image can be completely automated and the results of these automated analyses can be tabulated based on any number of criteria (particle size, shape, chemical composition, etc). Automated chemical

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imaging platforms have been developed that can run for hours in an unsupervised fashion.

This invention incorporates a comprehensive analysis approach that allows user's to carefully plan experiments and optimize instrument parameters and should allow the maximum amount of information to be extracted from chemical images so that the user can make intelligent decisions.

## EXAMPLE

### Overview

As the demand for high quality, low cost X-ray,  $\gamma$ -ray and imaging detector devices increases, there is a need to improve the quality and production yield of semiconductor materials used in these devices. One effective strategy for improving semiconductor device yield is through the use of better device characterization tools that can rapidly and nondestructively identify defects at early stages in the fabrication process. Early screening helps to elucidate the underlying causes of defects and to reduce downstream costs associated with processing defect laden materials that are ultimately scrapped. The present invention can be used to characterize tellurium inclusion defects in cadmium zinc telluride (CdZnTe) semiconductor materials based on near infrared imaging. With this approach, large area wafers can be inspected rapidly and non-destructively in two and three spatial dimensions by collecting NIR image frames at multiple regions of interest throughout the wafer using an automated NIR imaging system. The NIR image frames are subjected to image processing algorithms including background correction and image binarization. Particle analysis is performed on the binarized images to reveal tellurium inclusion statistics, sufficient to pass or fail wafers. In addition, data visualization software is used to view the tellurium inclusions in two and three spatial dimensions.

### Background

The present invention has been used to automatically inspect tellurium inclusions in CdZnTe. Compound semiconductors are challenging to fabricate. There are several steps along the manufacturing process in which defects can arise. The chemical nature associated with semiconductor defects often plays a vital role in device performance. Device fabrication and device processing defects can be difficult and time consuming to measure during manufacturing. Unfortunately, defective devices are often left undiagnosed until latter stages in the manufacturing process because of the inadequacy of the metrology tools being used. This results in low production yields and high costs which can be an impediment to growth in the semiconductor device market potential.

There is a general need in the semiconductor industry for metrology technologies that can nondestructively assess semiconductor material defects and ultimately increase manufacturing yields. A potential solution is to develop a high throughput screening system capable of fusing multiple chemical imaging modalities into a single instrument. Chemical imaging combines digital imaging and molecular spectroscopy for the chemical analysis of materials. A modality of based on near-infrared (NIR) chemical imaging can be used to inspect tellurium inclusions in CdZnTe compound semiconductor materials.

CdZnTe is a leading material for use in room temperature X-ray detectors,  $\gamma$ -ray radiation detectors and imaging devices. Applications for these devices include nuclear diagnostics, digital radiography, high-resolution astrophysical X-ray and  $\gamma$ -ray imaging, industrial web gauging and nuclear nonproliferation. These devices are often decorated with microscopic and macroscopic defects limiting the yield

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of large-size, high-quality materials. Defects commonly found in these materials include cracks, grain boundaries, twin boundaries, pipes, precipitates and inclusions. CdZnTe wafers are often graded based on the size and number of Te inclusion defects present.

The definition used by Rudolph and Muhlberg for tellurium inclusions (i.e., tellurium-rich domains in the 1–50  $\mu\text{m}$  size range that originate as a result of morphological instabilities at the growth interface as tellurium-rich melt droplets are captured from the boundary layer ahead of the interface) has been adopted and is used herein. There have been numerous studies on the composition and distribution of tellurium inclusions in CdZnTe material. It has been demonstrated that the presence of tellurium inclusions can impair the electronic properties of CdZnTe materials—consequently degrading the end-product device performance.

The current procedure used by low volume semiconductor manufacturers for characterizing tellurium inclusions in CdZnTe is labor intensive, susceptible to human error and provides little information on inclusions in the 1–5  $\mu\text{m}$  size scale. Inclusions are viewed and counted manually by a human operator using an IR microscope platform. When an inclusion is identified that is suspected to exceed a specified size limit, a Polaroid film photograph is taken. An overlay of a stage micrometer is laid over the photograph to determine the size. This analysis is relatively time consuming, often taking several minutes to characterize a region of interest from a large wafer.

The present invention can be used for automated characterization of microscale tellurium inclusions in CdZnTe based on volumetric NIR chemical imaging. The system takes advantage of the fact that CdZnTe is transparent to infrared wavelengths ( $>850\text{ nm}$ ). When viewing CdZnTe with an infrared focal plane array (IR-FPA) through a NIR LC imaging spectrometer, tellurium inclusions appear as dark, absorbing domains. The invention images wafers in two and three spatial dimensions capturing raw infrared images at each region of interest. Images are automatically background equilibrated, binarized and processed. The processed data provides particle statistical information such as inclusion counts, sizes, density, area and shape. The system provides a rapid method for characterizing tellurium inclusions as small as 0.5  $\mu\text{m}$  while virtually eliminating the subjectivity associated with manual inspection.

#### Sample Description

Tellurium-rich CdZnTe samples were produced by a commercial supplier (eV Products) for analysis. Samples containing high tellurium inclusion densities were purposely acquired to effectively demonstrate the capabilities of the automated tellurium inclusions mapping system. The CdZnTe materials were grown by the Horizontal Bridgeman (HB) method and contained a nominal zinc cation loading concentration of 4% and an average etch pit density of  $4 \times 10^4/\text{cm}^2$ . The materials displayed a face A  $\langle 111 \rangle$  orientation and were polished on both sides. Sample thicknesses ranged from approximately 1 mm to 15 mm. No further sample preparation was necessary for the automated tellurium inclusion mapping analysis.

#### Data Collection

Volumetric maps of the tellurium inclusions in the CdZnTe samples were obtained by first placing the sample on the XYZ-translational stage of the automated mapping system. NIR image frames were then captured through the LC imaging spectrometer at a wavelength that maximized the Te precipitate contrast relative to the surrounding CdZnTe matrix in the X-Y direction at multiple regions of

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interest across the samples. Depth profiling was achieved by translating the sample focus under the microscope at user-defined increments. This process was then repeated in an iterative fashion until the entire wafer was characterized.

#### 5 Data Processing

Once imaging data was collected, ChemImage was used to process the data. For each wafer, the software generates a background-corrected grayscale image, a binarized image using the threshold value selected for each frame of the image, a montage view of the binarized image and particle statistics. The particle statistics table includes information such as particle counts, particle sizes, particles densities, and a number of geometrical parameters such as particle area and particle aspect ratios.

#### 15 NIR Imaging

FIGS. 3 and 4, respectively, show a digital macro bright-field image and a raw NIR microscopic transmittance image of a CdZnTe semiconductor material with numerous tellurium inclusions. The left half of the wafer has been polished. The tellurium inclusions appear as dark spots in the microscopic NIR image. The raw NIR microscopic image was acquired using the automated near-infrared tellurium inclusion volumetric mapping system.

#### Background Correction and Image Binarization

The automated particle analysis begins by applying a background correction preprocessing routine to the raw image frames. One of the biggest problems with the raw images collected is the gradually varying background across each image frame. As a result, a particle in one area of a frame may have a higher intensity value than the background of another area of that frame.

FIGS. 5A–5D illustrate the difficulty associated with selecting a threshold value for an image with a widely varying background. In FIGS. 5A–5D, regions 1 and 2 have mean intensity values of approximately 2600 and 1950, respectively. The whole of region 1 is primarily a particle whereas region 2 is primarily background with a small particle in the center. FIG. 5A shows a raw NIR image frame collected from a single region of interest in a CdZnTe wafer. At wavelengths longer than approximately 850 nm, CdZnTe is transparent while tellurium inclusions remain opaque. A NIR image of the sample is light where there are no precipitates and dark where there are precipitates. In FIG. 5B, the threshold value is set low enough (value=1520) that the particle in region 2 is correctly identified, but most of the remaining particles are not found. In FIG. 5C, the threshold value is set high enough (value=2470) so that all particles are detected. Unfortunately, a large area of the frame is incorrectly identified as one very large particle. FIG. 5D displays the case in which the threshold is set to an intermediate value (value=1960). Many of the particles are correctly identified, but the particle in region 2 is identified as being larger than it actually is.

To address this issue, a background correction step is used to force the background to be essentially constant across a given image frame. The procedure applies a moving window across the image frame and smoothes the resulting background before subtracting it from the frame. Other operations such as low pass filtering and selective removal of bad camera pixels are also applied.

The second step in the automated particle analysis is the selection of the threshold value resulting in the binarized image which best reflects the number and size of particles actually present in the sample being imaged. A human operator would typically approach this problem by trying multiple threshold values and comparing the resulting binarized images to the actual image to see which binarized

image best matches their perception of the particles in the actual image. The algorithm employed by the NIR chemical imaging microscope system takes essentially the same approach. A series of threshold values are used to generate binarized images. Each binarized image is submitted to a routine that finds the particles present in the image. A set of particle morphology rules was developed to determine the point at which the threshold value identifies the particles consistent with results obtained by a trained human operator. This threshold value is then further refined with using derivative operations.

FIGS. 6A–6C show montage views of raw, background-corrected, and binarized NIR image frames, respectively, corresponding to four adjacent regions of interest from a CdZnTe wafer. A visual inspection of these images suggests that the particle analysis adequately identifies the particles in an automated fashion.

Volumetric Reconstruction and Visualization

It is of particular interest to the semiconductor manufacturing industry to view defects, including tellurium inclusions in this example, in a three dimensional volumetric view. Individual binarized image frames generated at discrete axial planes of focus have been reconstructed into a volumetric view allowing users to view tellurium inclusions in three-dimensional space.

FIG. 7 shows a 3D volumetric view of tellurium inclusions in CdZnTe generated from 50 individual image slices. FIG. 7 is constructed using a nearest neighbors computational approach for volume reconstruction. Improved results can be obtained using more sophisticated strategies that deconvolve the entire image volume using iterative deconvolution approaches. The staring time of the sensor used to gather the volumetric data was less than 1 sec. The total acquisition time for the data generated in this figure was well under a minute. Note how the inclusions tend to form in planes described as veils. These veils are believed to be subgrain boundaries within the CdZnTe material. Grain boundaries provide low energy nucleation sites for the inclusions to form during the growth process.

Table 1 provides tabulated statistical information on the volumetric data shown in FIG. 7.

TABLE 1

Parameters	Particle Statistics					
	Slice Number and Depth (μm)					
	0 (0)	10 (89.77)	20 (189.52)	30 (289.26)	40 (389.01)	50 (488.75)
# of Inclusions	25	30	27	24	25	36
Mean Diameter (μm)	12.12	11.38	12.75	15.70	12.89	13.73
Density (Inclusions/cm <sup>2</sup> )	4368	5241	4717	4193	4368	6289
Area (μm <sup>2</sup> )	97.48	73.78	91.67	119.25	96.29	98.15
Perimeter (μm)	40.40	37.32	43.27	50.72	41.93	43.98
Shape Factor	0.60	0.60	0.58	0.53	0.60	0.55
Maximum Chord Length	12.12	11.38	12.75	15.70	12.89	13.73
Feret 1 Diameter	9.17	9.56	11.33	12.64	10.48	10.16
Feret 2 Diameter	10.26	9.01	10.10	12.18	10.37	11.60
Aspect Ratio	1.02	1.19	1.16	1.08	1.02	0.95

Defects such as tellurium inclusions affect the electrical properties in CdZnTe semiconductor materials, degrading end-product device performance. Having the ability to rapidly and non-invasively identify and quantify tellurium inclusion defects at critical stages in the fabrication process provides semiconductor manufacturers with information that will enable them to optimize the manufacturing process and reduce production costs. The Automated NIR Volumetric Mapping System described here is capable of providing such information. The system provides qualitative and quan-

titative information about tellurium inclusions present in CdZnTe wafers in two and three spatial dimensions. This system boasts improved spatial resolution (~0.5 μm) compared to systems currently used by many semiconductor manufacturers and it virtually eliminates the subjectivity associated with human counting and sizing measurements. Whole wafers are capable of being characterized in minutes.

While in the above example, the present invention has been demonstrated in connection with the characterization of semiconductors, it is to be expressly understood that the present invention can also be used in the characterization of other materials including, but not limited to, food and agricultural products, paper products, pharmaceutical materials, polymers, thin films and in medical uses.

Although present preferred embodiments of the invention have been shown and described, it should be distinctly understood that the invention is not limited thereto but may be variously embodied within the scope of the following claims.

We claim:

1. A near infrared radiation chemical imaging system comprising:
  - a) an illumination source for illuminating an area of a sample using light in the near infrared radiation wavelength;
  - b) a device for collecting a spectrum of near infrared wavelength radiation light transmitted, reflected, emitted or scattered from said illuminated area of said sample and producing a collimated beam therefrom;
  - c) a near infrared imaging spectrometer for selecting a near infrared radiation image of said collimated beam; and
  - d) a detector for collecting said filtered near infrared images.
2. The system of claim 1 wherein said illumination source is one of a quartz tungsten halogen lamp, a tunable laser, a metal halide lamp, and a xenon arc lamp.
3. The system of claim 1 wherein said device for collecting is one of a refractive type infinity-corrected near infrared optimized microscope objective, a refractive fixed tube length microscope objective, and a reflecting microscope objective.
4. The system of claim 1 wherein said near infrared imaging spectrometer is selected from the group consisting of Lyot liquid crystal tunable filters; Evans Split-Element liquid crystal tunable filters; Solc liquid crystal tunable filters; Ferroelectric liquid crystal tunable filters; Liquid crystal Fabry Perot filters; a hybrid filter formed from a combination of liquid crystal tunable filters; and a combination of a liquid crystal tunable filter and a fixed bandpass and bandreject filters.

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5. The system of claim 1 wherein said detector is a near infrared radiation focal plane array detector.

6. The system of claim 5 wherein said detector is selected from the group consisting of indium gallium arsenide, platinum silicide, indium antimonide, palladium silicide, indium germanide, and mercury cadmium telluride.

7. The system of claim 1 further comprising a visible wavelength imagery system.

8. The system of claim 7 wherein said visible imagery system comprises:

- a) an illumination source for illuminating an area of said sample using light in the visible optical wavelengths; and
- b) a device for detecting said visible wavelength light from said illuminated area of said sample.

9. The system of claim 8 wherein said device for detecting said visible wavelength light comprises an analog and digital detector based on at least one of a silicon charge-coupled device detector and a silicon CMOS detectors.

10. The system of claim 8 further comprising a processor for producing a near infrared radiation chemical image of said sample.

11. The system of claim 8 further comprising an algorithm for combining the near infrared and visible image data.

12. A chemical imaging system comprising:

- a) an illumination source for illuminating an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength;
- b) a device for collecting a spectrum of near infrared wavelength radiation light transmitted, reflected, emitted or scattered from said illuminated area of said sample and producing a collimated beam therefrom;
- c) a near infrared imaging spectrometer for selecting a near infrared radiation image of said collimated beam;
- d) detector for collecting said filtered near infrared images; and
- e) a device for detecting said visible wavelength light from said illuminated area of said sample.

13. A chemical imaging method comprising the steps of:

- a) illuminating an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength;
- b) collecting a spectrum of near infrared wavelength radiation light transmitted, reflected, emitted or scattered from said illuminated area of said sample and producing a collimated beam therefrom;
- c) filtering said collimated beam to produce a near infrared radiation image of said collimated beam while

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simultaneously detecting said optical wavelength light from said illuminated area of said sample;

- d) collecting said filtered near infrared images; and
- e) processing said collected near infrared images to produce a chemical image of said sample.

14. A method for producing a volumetric image of a sample comprising the steps of:

- a) incorporating a refractive image formation optic exhibiting a chromatic response in the optical path of the microscope before the near infrared detector;
- b) collecting images of said sample at a plurality of near infrared wavelengths through said objective at a fixed focus condition; and
- c) processing said collected images to reconstruct a depth resolved image of said sample.

15. A method for chemically analyzing a sample comprising the steps of:

- a) seeding said sample with a plurality of analytes having at least one of a known composition, structure and concentration;
- b) collecting a plurality of spatially-resolved spectra for said plurality of analytes;
- c) producing a plurality of chemical images of said sample containing said plurality of analytes; and
- d) processing said plurality of chemical images to generate a chemical image of said sample.

16. The method of claim 15 wherein said processing step comprises at least one of:

- a) correcting the image by dividing a near infrared image of said sample by a near infrared image of a background of said image to produce a resulting ratioed image;
- b) normalizing the divided image by dividing each intensity value at every pixel in the image by the vector norm for its corresponding pixel spectrum, said vector norm being the square root of the sum of the squares of pixel intensity values for each pixel spectrum;
- c) processing said image using a cosine correlation analysis method wherein each pixel spectrum is treated as a projected vector in n-dimensional space, wherein n is the number of wavelengths sampled in the image; and
- d) processing said image using a principal component analysis method wherein a least squares fit is drawn through the maximum variance in the n-dimensional dataset.

\* \* \* \* \*

PATENT  
Attorney Docket No. 56751-5008RE

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: )  
U.S. Patent No. 6,734,962 )  
Issue Date: May 11, 2004 )  
Filing Date: October 12, 2001 )  
Reissue Application No.: (Not Assigned) )  
For: NEAR INFRARED CHEMICAL IMAGING )  
MICROSCOPE )

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**PRELIMINARY AMENDMENT**

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Mail Stop Reissue  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Prior to the examination of the above-identified application on the merits, please enter the following amendments.

Amendments to the Specification are reflected on page 2 of this paper.

Amendments to the Claims are reflected on page 3 of this paper.

Remarks begin on page 5 of this paper.

**EXPRESS MAIL CERTIFICATE (37 C.F.R. § 1.10)**

Express Mail Label No. EV260286646US

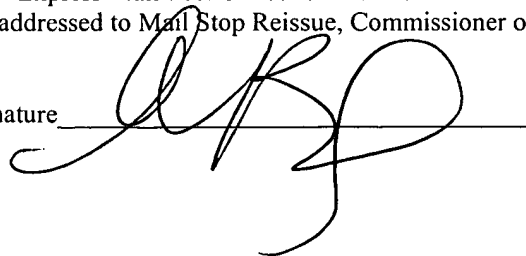
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I hereby certify that this paper, and the papers and/or fees referred to herein as transmitted, submitted or enclosed, are being deposited with the U.S. Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to Mail Stop Reissue, Commissioner of Patents P.O. Box 1450 Alexandria, VA 22313-1450.

Name Alison B. Weisberg

Signature



**IN THE SPECIFICATION**

Please replace the Abstract with the following:

A chemical imaging system is provided which uses a near infrared radiation microscope. The system includes an illumination source which illuminates an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength. A multitude of spatially resolved spectra of transmitted, reflected[, ] or emitted [or scattered] near infrared wavelength radiation light from the illuminated area of the sample is collected and a collimated beam is produced therefrom. A near infrared imaging spectrometer is provided for selecting [a] near infrared radiation images of the collimated beam. The spectrometer comprises a liquid crystal tunable filter. The [filtered] selected images are collected by a detector for further processing. The visible wavelength light from the illuminated area of the sample is simultaneously detected providing for the simultaneous visible and near infrared chemical imaging analysis of the sample. Two efficient means for performing three dimensional near infrared chemical imaging microscopy are provided.

**IN THE CLAIMS**

Please amend claims 1, 12, and 13.

1. (Amended) A near infrared radiation chemical imaging system comprising:

- a) an illumination source for illuminating an area of a sample using light in the near infrared radiation wavelength;
- b) a device for collecting a spectrum of near infrared wavelength radiation light transmitted, reflected[,] or emitted [or scattered] from said illuminated area of said sample and producing a collimated beam therefrom;
- c) a near infrared imaging spectrometer for selecting [a] near infrared radiation images of said collimated beam, wherein the spectrometer comprises a liquid crystal tunable filter; and
- d) a detector for collecting said selected [filtered] near infrared images.

12. (Amended) A chemical imaging system comprising:

- a) an illumination source for illuminating an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength;
- b) a device for collecting a spectrum of near infrared wavelength radiation light transmitted, reflected[,] or emitted [or scattered] from said illuminated area of said sample and producing a collimated beam therefrom;
- c) a near infrared imaging spectrometer for selecting [a] near infrared radiation images of said collimated beam, wherein the spectrometer comprises a liquid crystal tunable filter;
- d) detector for collecting said selected [filtered] near infrared images; and

e) a device for detecting said visible wavelength light from said illuminated area of said sample.

13. (Amended) A chemical imaging method comprising the steps of:

- a) illuminating an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength;
- b) collecting a spectrum of near infrared wavelength radiation light transmitted, reflected[,] or emitted [or scattered] from said illuminated area of said sample and producing a collimated beam therefrom;
- c) filtering said collimated beam to produce [a] near infrared radiation images of said collimated beam while simultaneously detecting said optical wavelength light from said illuminated area of said sample, wherein the filtering is performed using a liquid crystal tunable filter;
- d) collecting said filtered near infrared images; and
- e) processing said collected near infrared images to produce a chemical image of said sample.

**REMARKS**

The Abstract has been amended to secure substantial correspondence between the claims, the remainder of the specification and the drawings, in accordance with 37 C.F.R. § 1.173(f).

**Statements of Status/Support for Changes to the Claims under 37 C.F.R. §1.173(c)**

The status of the claims is as follows. Claims 1-16 were allowed in the parent application leading to U.S. Patent No. 6,734,962 (the “’962 patent”). Claims 1, 12, and 13 are amended by way of this amendment. The basis for the amendment is as follows.

As issued, claims 1 and 12 of the ‘962 patent are directed to a near infrared radiation chemical imaging system that includes “a device for collecting a spectrum of near infrared wavelength radiation light transmitted, reflected, emitted or scattered from said illuminated area of said sample and producing a collimated beam therefrom”. Similarly, claim 13 is directed to a chemical imaging method that includes “collecting a spectrum of near infrared wavelength radiation light transmitted, reflected, emitted or scattered from said illuminated area of said sample and producing a collimated beam therefrom.”

Further, claims 1 and 12 of the issued ‘962 patent refer to a near infrared imaging spectrometer, without further description of the type of filter included in the spectrometer. Similarly, claim 13 includes a filtering step, without reference to the type of filter used to perform the step.

Two articles were submitted to the Patent and Trademark Office for consideration during the prosecution of the ‘962 patent: Patrick J. Treado, Ira W. Levin, and E. Neil Lewis, “Indium Antimonide (InSb) Focal Plan Array (FPA) Detection for Near-Infrared

Imaging Microscopy”, Applied Spectroscopy 48, 607 (1994) (“Acousto-Optic Tunable Filter Reference”); and H. Morris, C. Hoyt, P. Filler and P. Treado, “Liquid Crystal Tunable Filter Raman Chemical Imaging”, Vol. 50, Applied Spectroscopy, No. 6, pp. 805-811 (1996) (“Raman Spectroscopy Reference”). The Acousto-Optic Tunable Filter Reference and the Raman Spectroscopy Reference are referred to collectively herein as Prior Art.

The Acousto-Optic Tunable Filter Reference discloses near infrared spectroscopy using a refractive optical microscope and an acousto-optic tunable filter to display spectroscopic images of biological and polymeric systems. The Raman Spectroscopy Reference discloses use of a liquid crystal tunable filter suitable for high definition Raman chemical imaging. Raman chemical imaging involves Raman scattering and measures the energy (i.e., wavelength) difference between the known incident light and the light that is scattered upon striking a sample (i.e., inelastic scattering). The resulting Raman scattered light is referred to as inelastically scattered light.

As a result of the inclusion of the term “scattered”, and failure to specify that the type of filter used is a “liquid crystal tunable filter” in claims 1, 12 and 13, it appears that the ‘962 patent claims more than the applicants were entitled to claim in claims 1, 12 and 13 in view of the Prior Art.

The applicants failed to appreciate this error during the prosecution of the patent application. However, the oversight was not a result of any deceptive intent. In fact, the Prior Art was submitted by the applicants during the prosecution of the ‘962 patent, was considered by the examiner, and is listed on the face of the ‘962 patent.

Claims 1, 12 and 13 of the present reissue application have been amended such that they claim subject matter that does not read on the Prior Art, as follows. Element (b) of claims 1 and 12, and step (b) of claim 13, include the term “scattered”. Claims 1, 12 and 13 have been amended to delete this term. Support for this amendment can be found in the ‘962 patent at column 3, line 22 – 25, column 4, lines 57 – 67, and in the claims as originally filed in the application that matured into the ‘962 patent. Element (c) of claims 1 and 12 fails to specify the type of filter included in the spectrometer. Similarly, claim 13 fails to indicate the type of filter that performs the filtering step (c). Claims 1, 12 and claim 13 have been amended to specify, respectively, that the “spectrometer comprises a liquid crystal tunable filter” and the “filtering is performed using a liquid crystal tunable filter.” Support for this amendment can be found in the ‘962 patent at column 4, lines 45 – 56 and in more detail at column 5, lines 31 – 41.

In addition, the reissue claims seek to remove the following apparent typographical errors which were discovered during the preparation of the present reissue application. The following amendments to the claims have thus been made in order to bring the claims into compliance with 35 U.S.C. § 112, second paragraph.

Element (d) of claim 1 recites “a detector for collecting said filtered near infrared images”, referring back to element (c) which recites “a near infrared imaging spectrometer for selecting a near infrared radiation image” (emphasis added). Thus, element (c) of claim 1 has been amended to include the plural term “images” and element (d) of claim 1 has been amended to include the term “said selected near infrared images” rather than “said filtered near infrared images”, thereby providing proper antecedent basis in this claim.

Element (d) of claim 12 recites “a detector for collecting said filtered near infrared images”, referring back to element (c) which recites “a near infrared imaging spectrometer for selecting a near infrared radiation image” (emphasis added). Thus, element (c) of claim 12 has been amended to include the plural term “images” and element (d) of claim 12 has been amended to include the term “said selected near infrared images” rather than “said filtered near infrared images”, thereby providing proper antecedent basis in this claim.

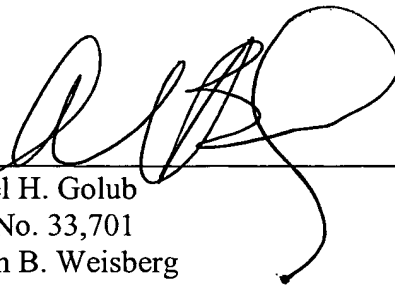
Step (d) of claim 13 recites “collecting said filtered near infrared images”, referring back to element (c) which recites “filtering said collimated beam to produce a near infrared radiation image”. Thus, step (c) of claim 13 has been amended to include the plural term “images”, thereby providing proper antecedent basis for this claim.

Accordingly, claims 1, 12, and 13 have been amended to reflect these corrections. Claims 1-16 are now pending.

In accordance with 37 C.F.R. § 1.178(b), applicants hereby call to the attention of the Patent Office the following proceeding in which the '962 patent is currently involved: Cambridge Research & Instrumentation, Inc., et al. v. ChemImage Corporation et al., action no. 05 10367(RWZ) (D. Mass). This action is currently pending. A complaint has been filed, a copy of which is attached hereto. The applicants request that this reissue application be examined at this time and not be stayed pending the outcome of the litigation.

The applicants respectfully request consideration of the subject application in view of the above amendments and remarks. Applicants looks forward to a favorable Office Action on the merits.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'D. Golub', is written over a horizontal line.

Daniel H. Golub  
Reg. No. 33,701  
Alison B. Weisberg  
Reg. No. 45,206  
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Dated: 4/11/05



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
11/103.423	04/11/2005	Patrick J. Treado	5675-5008RE	2434

7590 09/25/2006  
 Daniel Golub  
 1701 Market Street  
 Philadelphia, PA 19103

EXAMINER
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LAUCHMAN, LAYLA G

ART UNIT	PAPER NUMBER
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2877

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

11/103,423

Applicant(s)

TREADO ET AL.

Examiner

L. G. Lauchman

Art Unit

2877

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 12-16 is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) 7-11 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: ____  |

Continuation Sheet (PTOL-326)

Application No. 11/103,423

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :05/09/2005; 05/18/2005;06/01/2005; 10/13/2005;11/04/2005.

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***Reissue Applications***

While there is a stay of the concurrent litigation related to this reissue application, action in this reissue application will NOT be stayed or suspended because a stay of that litigation is in effect for the purpose of awaiting the outcome of these reissue proceedings. Due to the related litigation status of this reissue application, EXTENSIONS OF TIME UNDER THE PROVISIONS OF 37 CFR 1.136(a) WILL NOT BE PERMITTED.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoyt et al (US 5,943,129) ("Hoyt"), and in view of Soenksen (US 6,711,283).

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As to Claim 1, Hoyt discloses a an imaging system comprising: a) an illumination source (Fig. 15, reference 11) for illuminating an area of a sample (20) using light in the near infrared radiation wavelength (col. 16, lines 61-64); b) a device 16 for collecting a spectrum of near infrared wavelength radiation light emitted from said illuminated area of said sample; c) a near infrared imaging spectrometer (120) for selecting near infrared radiation images, wherein the spectrometer comprises a liquid crystal tunable filter (col. 5, line48 through col. 6, line 8); and d) a detector for collecting said selected near infrared images (25).

Hoyt is silent about the device being able to produce a collimated beam therefrom. Soenksen discloses an objective lens 16 being able to produce collimated light onto the light responsive elements of the scan camera 18 (see Fig. 1 and 2, col. 9, lines 12 - 50). It would have been obvious to one skilled in the art at the time the invention was made to provide the system of Hoyt with the device or a microscope objective that would collimate the light onto the spectrometer, in order to minimize chromatic aberration and maximize throughput.

As to Claim 2, the illumination source of Hoyt is a laser or a xenon lamp, or an arc lamp (see col. 5, lines 16-20).

As to Claim 3, the device for collecting in the invention of Hoyt is a not refractive type infinity-corrected optimized microscope objective. Soenksen discloses a microscope objective lens 16, which is of the infinity corrected type. It would have been obvious to one skilled in the art at the time the invention was made to provide the system of Hoyt with the infinity-corrected lens that would collimate the light onto the spectrometer, in order to minimize chromatic aberration, maximize throughput and reduce cost of the conventional tube lens.

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As to Claim 4, the infrared imaging spectrometer of Hoyt is and a combination of a liquid crystal tunable filter and a fixed bandpass and bandreject filters (see col. 6, lines 2 – 8).

As to Claims 5 and 6, the detector of Hoyt is a infrared radiation focal plane array detector (col. 15, lines 16-24), and as to the detector being of indium gallium arsenide, the InGaAs based charge-coupled devices are well known as sensitive to near-infrared radiation in the range 900-1700 nm. (see US patent 6,373,567 to Wise et al). It would have been obvious to one skilled in the art at the time the invention was made to have an InGaAs based CCD detector in the invention of Hoyt to provide multi-wavelength detection.

***Allowable Subject Matter***

Claims 7-11 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The following is a statement of reasons for the indication of allowable subject matter: The prior art of record taken along or in combination, fails to disclose or render obvious a visible wavelength imagery system, in combination with the rest of the limitations of the claim 1.

Claims 12-16 are allowed.

As to Claim 12, the prior art of record taken along or in combination, fails to disclose or render obvious a device for detecting said visible wavelength light from said illuminated area of said sample, in combination with the rest of the limitations of the claim.

As to Claim 13, the prior art of record taken along or in combination, fails to disclose or render obvious illuminating an area of a sample using light in the near infrared radiation

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wavelength and light in the visible wavelength and processing said collected near infrared images to produce a chemical image of said sample, in combination with the rest of the limitations of the claim.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to L. G. Lauchman whose telephone number is (571) 272-2418. The examiner's normal work schedule is 8:00am to 4:30pm (EST), Monday through Friday. If attempts to reach examiner by the telephone are unsuccessful, the examiner's supervisor Gregory J. Toatley, Jr. can be reached on (571) 272-2059, ext. 77.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Page 6

Any inquiry of a general nature or relating to the status of this application should be directed to the TC receptionist whose telephone number is (571) 272-1562.

A handwritten signature in black ink, appearing to read 'L. G. Lauchman', with a large, stylized initial 'L'.

L. G. Lauchman  
Primary Examiner  
Art Unit 2877

September 11, 2006

PATENT  
Attorney Docket No. 56751-5008RE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Reissue Application No.: 11/103,423

Filed: April 11, 2005

For: NEAR INFRARED CHEMICAL IMAGING  
MICROSCOPE

Examiner: Lauchman, Layla G.

RECEIVED  
CENTRAL FAX CENTER

OCT 31 2006

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AMENDMENT

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

The following is submitted in response to the Official Action dated September 25, 2006.

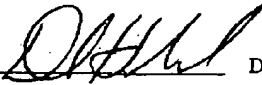
Amendments to the Claims begin on page 2 of this paper.

Remarks begin on page 6 of this paper.

CERTIFICATE OF FAX TRANSMISSION (37 C.F.R. § 1.8)

I hereby certify that this paper, and the papers and/or fees referred to herein as transmitted, submitted or enclosed, are being faxed on the date shown below to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, at fax number 571-273-8300.

Name Daniel H. Golub

Signature 

Date of Deposit: October 16, 2006

Attorney Docket No. 56751-5008 RE

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**IN THE CLAIMS**

1-6. (Cancelled)

7. (Amended) A near infrared radiation chemical imaging system comprising:

a) an illumination source for illuminating an area of a sample using light in the near infrared radiation wavelength;

b) a device for collecting a spectrum of near infrared wavelength radiation light transmitted, reflected or emitted from said illuminated area of said sample and producing a collimated beam therefrom;

c) a near infrared imaging spectrometer for selecting near infrared radiation images of said collimated beam, wherein the spectrometer comprises a liquid crystal tunable filter; and

d) a detector for collecting said selected near infrared images;

[The system of claim 1] further comprising a visible wavelength imagery system.

8. (Original) The system of claim 7 wherein said visible imagery system comprises: a) an illumination source for illuminating an area of said sample using light in the visible optical wavelengths; and b) a device for detecting said visible wavelength light from said illuminated area of said sample.

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9. (Original) The system of claim 8 wherein said device for detecting said visible wavelength light comprises an analog and digital detector based on at least one of a silicon charge-coupled device detector and a silicon CMOS detectors.

10. (Original) The system of claim 8 further comprising a processor for producing a near infrared radiation chemical image of said sample.

11. (Original) The system of claim 8 further comprising an algorithm for combining the near infrared and visible image data.

12. (Amended) A chemical imaging system comprising:

- a) an illumination source for illuminating an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength;
- b) a device for collecting a spectrum of near infrared wavelength radiation light transmitted, reflected[, ] or emitted [or scattered] from said illuminated area of said sample and producing a collimated beam therefrom;
- c) a near infrared imaging spectrometer for selecting [a] near infrared radiation images of said collimated beam, wherein the spectrometer comprises a liquid crystal tunable filter;
- d) detector for collecting said selected [filtered] near infrared images; and
- e) a device for detecting said visible wavelength light from said illuminated area of said sample.

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Page 4

13. (Twice amended) A chemical imaging method comprising the steps of:

- a) illuminating an area of a sample using light in the near infrared radiation wavelength and light in the visible wavelength;
- b) collecting a spectrum of near infrared wavelength radiation light transmitted, reflected[, ] or emitted [or scattered] from said illuminated area of said sample and producing a collimated beam therefrom;
- c) filtering said collimated beam to produce [a] near infrared radiation images of said collimated beam while simultaneously detecting said [optical] visible wavelength light from said illuminated area of said sample, wherein the filtering is performed using a liquid crystal tunable filter;
- d) collecting said filtered near infrared images; and
- e) processing said collected near infrared images to produce a chemical image of said sample.

14. (Original) A method for producing a volumetric image of a sample comprising the steps of: a) incorporating a refractive image formation optic exhibiting a chromatic response in the optical path of the microscope before the near infrared detector; b) collecting images of said sample at a plurality of near infrared wavelengths through said objective at a fixed focus condition; and c) processing said collected images to reconstruct a depth resolved image of said sample.

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Page 5

15. (Original) A method for chemically analyzing a sample comprising the steps of: a) seeding said sample with a plurality of analytes having at least one of a known composition, structure and concentration; b) collecting a plurality of spatially-resolved spectra for said plurality of analytes; c) producing a plurality of chemical images of said sample containing said plurality of analytes; and d) processing said plurality of chemical images to generate a chemical image of said sample.

16. (Original) The method of claim 15 wherein said processing step comprises at least one of: a) correcting the image by dividing a near infrared image of said sample by a near infrared image of a background of said image to produce a resulting ratioed image; b) normalizing the divided image by dividing each intensity value at every pixel in the image by the vector norm for its corresponding pixel spectrum, said vector norm being the square root of the sum of the squares of pixel intensity values for each pixel spectrum; c) processing said image using a cosine correlation analysis method wherein each pixel spectrum is treated as a projected vector in n-dimensional space, wherein n is the number of wavelengths sampled in the image; and d) processing said image using a principal component analysis method wherein a least squares fit is drawn through the maximum variance in the n-dimensional dataset.

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### REMARKS

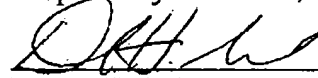
The status of the claims is as follows. Claims 1-6 were rejected for obviousness in the last official action and have been cancelled. Claims 7-16 were allowed in the last official action and are pending.

Claim 7 has been amended to include all of the limitations of deleted claim 1. Support for the limitations added to claim 7 can be found, for example, in the Abstract of U.S. Patent No. 6,734,962.

Claim 13 has been amended to correct a formal error that Applicant identified when responding to the outstanding official action. As previously worded, step (c) of claim 13 included a reference to said "optical" wavelength light. However, there was no antecedent basis in the claim for this term. Applicant has replaced "optical" with "visible" in claim 13 to correct this informality. Support for this amendment to claim 13 can be found, for example, in claim 13 of U.S. Patent No. 6,734,962.

In view of the foregoing, Applicant submits that the application is in condition for allowance.

Respectfully submitted,



Daniel H. Golub  
Reg. No. 33,701  
Morgan, Lewis & Bockius LLP  
1701 Market Street  
Philadelphia, PA 19103  
(215)963-5055 (Phone)  
(215)963-5001 (Fax)

Dated: October 16, 2006

**Notice of Allowability**

Application No.

11/103,423

Examiner

L. G. Lauchman

Applicant(s)

TREADO ET AL.

Art Unit

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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 1/31/07.
2. ☒ The allowed claim(s) is/are 7-16.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date See Continuation Sheet
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

**Continuation Sheet (PTOL-37)**

**Application No. 11/103,423**

Continuation of Attachment(s) 3. Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date: 10/13/2006, 11/20/2006.

## **DETAILED ACTION**

### ***Information Disclosure Statement***

The information disclosure statement filed on November 20, 2006 fails to comply with the provisions of 37 CFR 1.97, 1.98(C) § 609 because it is missing the date of the reference. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

The information disclosure statement filed with protest under 37 C.F.R. 1.291, submitted on 10/13/2006 by a third party, has been placed in the application file, but the information referred to therein has not been considered, since the information is not related to the prior art.

### ***Allowable Subject Matter***

Claims 7-16 are allowed.

The following is an examiner's statement of reasons for allowance:

As to Claim 1, the prior art of record, taken alone or in combination, fails to disclose or render obvious a near infrared imaging spectrometer for selecting near

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infrared radiation images of said collimated beam, wherein the spectrometer comprises a liquid crystal tunable filter; and a detector for collecting said selected near infrared images; further comprising a visible wavelength imagery system, in combination with the rest of the limitations of the claim.

As to Claim 12, the prior art of record, taken along or in combination, fails to disclose or render obvious a near infrared imaging spectrometer for selecting near infrared radiation images of said collimated beam, wherein the spectrometer comprises a liquid crystal tunable filter; detector for collecting said selected near infrared images; and a device for detecting said visible wavelength light from said illuminated area of said sample, in combination with the rest of the limitations of the claim.

As to Claim 13, the prior art of record, taken along or in combination, fails to disclose or render obvious filtering said collimated beam to produce a near infrared radiation images of said collimated beam while simultaneously detecting visible wavelength light from said illuminated area of said sample, wherein the filtering is performed using a liquid crystal tunable filter; collecting said filtered near infrared images; and processing said collected near infrared images to produce and display a chemical image of said sample, in combination with the rest of the limitations of the claim.

As to Claim 14, the prior art of record, taken along or in combination, fails to disclose or render obvious collecting images of said sample at a plurality of near infrared wavelengths through said objective at a fixed focus condition and processing said collected images to reconstruct and display a depth resolved image of said sample, in combination with the rest of the limitations of the claim.

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As to Claim 15, the prior art of record, taken along or in combination, fails to disclose or render obvious producing a plurality of chemical images to generate a chemical image of said sample containing said plurality of analytes and processing said plurality of chemicals images to generate a chemical image of said sample and displaying said chemical image, in combination with the rest of the limitations of the claim.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to L. G. Lauchman whose telephone number is (571) 272-2418. The examiner's normal work schedule is 8:00am to 4:30pm (EST), Monday through Friday. If attempts to reach examiner by the telephone are unsuccessful, the examiner's supervisor Gregory J. Toatley, Jr. can be reached on (571) 272-2059, ext. 77.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

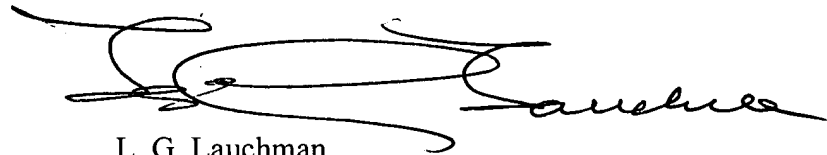
Application/Control Number: 11/103,423

Page 5

Art Unit: 2877

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

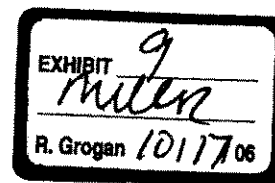
Any inquiry of a general nature or relating to the status of this application should be directed to the TC receptionist whose telephone number is (571) 272-1562.

A handwritten signature in black ink, appearing to read 'Lauchman', with a large, stylized initial 'L'.

L. G. Lauchman  
Primary Examiner  
Art Unit 2877

3/13/2007

\*\*\*



## SMALL BUSINESS INNOVATION RESEARCH (SBIR) PHASE II REPORT COVER SHEET

NSF AWARD NUMBER: DMI-9703950		DATE: 10 January 2000	
PROJECT TITLE: High-Definition Raman Imaging Microscope			
PERIOD COVERED BY THIS REPORT: Sept. 1, 1997 - Dec. 30, 1999		PRINCIPAL INVESTIGATOR: Peter J. Miller	
COMPANY NAME: Cambridge Research & Instrumentation, Inc.			
COMPANY ADDRESS: 80 Ashford Street Boston, MA 02134			
TELEPHONE NUMBER: 617-787-5700		FAX NUMBER: 617-787-4488	

Please check as appropriate:

☐ Progress Report\*☒ Final Report\*

\* Report content requirements are identified in Article 5 of the SBIR Phase II Grant General Conditions (9/95). This Cover Sheet is required for submission of all reports. Reports should be attached to this Cover Sheet.

**Acknowledgment of NSF support and disclaimer:**

*This material is based upon work supported by the National Science Foundation under Award Number [redacted]. Any opinions, findings, and conclusions or recommendations expressed in this publication are those of the author(s) and do not necessarily reflect the views of the National Science Foundation.*

**Certifications:**

I certify that the Principal Investigator currently is ☒ , is not ☐ , "primarily employed" by the grantee organization as defined in the SBIR Solicitation.

I certify that the work under this project has ☐ , has not ☒ , been submitted for funding to another Federal agency and that it has ☐ , has not ☒ , been funded under any other Federal grant, contract, or subcontract.

I certify that to the best of my knowledge the work for which payment is hereby requested was performed in accordance with the award terms and conditions and that payment is due and has not been previously requested.

I certify that to the best of my knowledge (1) the statements herein(excluding scientific hypotheses and scientific opinions) are true and complete, and (2) the text and graphics in this report as well as any accompanying publications or other documents, unless otherwise indicated, are the original work of the signatories or individuals working under their supervision. I understand that the willful provision of false information or concealing a material fact in this report or any other communication submitted to NSF is a criminal offense (U.S. Code, Title 18, Section 1001).

Authorized Grantee Representative Signature: Peter J. MillerDate: 1/10/00P.I. Signature: PMDate: 1/10/00

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**Final Report - DMI 9703950**

The project has been completed successfully at the end of December 1999, taking advantage of an unfunded extension period of up to six months beyond the nominal completion date of August 31st, 1999.

This report contains information on the final reporting interval of 1 March 1999 - 30 December 1999, followed by a summary of results for the entire project.

**Activity during the final reporting period**

During this period, the number of person-months expended by the PI is 1.7, and 1.7 by other project personnel at CRI. Subcontractor services representing \$5760 for research assistant support were provided by ChemIcon, and Dr. Patrick Treado consulted for 19 days at a total expense of \$8064. This information is captured in the SBIR Phase II Semiannual Reporting Format on an attached sheet.

**Technical report (final reporting period)**

During this period, the main technical objectives were to assess the filter design for improved off-axis performance, to bring the multispectral analysis software to conclusion, and to finish the application assessment. Also, the imaging spectrometers were repaired and reconfigured following the failure of one of the detector arrays involved.

**New filter design**

As noted in the previous report, a design was developed for use in Phase III, to achieve improved off-axis performance as well as improved transmission. The design utilized fewer split-element Evans stages, replacing them with simpler wide-field stages, constructed with achromatic half-wave plates made of z-compensated biaxial polycarbonate films. The same films are slated to replace Mylar as a retarder material throughout the filter, as they exhibit essentially no shift in retardance as a function of viewing angle.

There is a double benefit to this improved design. First, where Mylar was used as the central element in a split-element stage, its relatively poor off-axis response degraded off-axis contrast; this is eliminated by use of the z-compensated films, so off-axis response of these split-element stages appears to be essentially undegraded relative to that of a simple Lyot stage. Second, two stages which utilized  $\text{LiNbO}_3$  as the central element in split-element Evans design were replaced with wide-field elements comprising equal-valued retarders sandwiched about an achromatic half-wave plate. Conventional three-layer Pancharatnam designs are sufficient to compensate either of the two spectral ranges involved: 500 - 750 nm, or 650 - 1050 nm. In this setting, where non-achromaticity is manifest as reduced filter efficiency rather than reduced filter contrast, a 2% ripple is permissible; this is readily attained using NRZ-300 material (visible) or NRZ-400 material (near-IR) oriented at angles of  $[-29^\circ, +29^\circ, -29^\circ]$ . When constructed of z-compensated films, these have the property not only of achromaticity, but also of

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wideviewing angle. Finally, one low-order filter stage was eliminated as redundant.

The net effect of these changes is a decrease by three in the number of liquid crystal cells, and an increase by one in the number of polarizers. Since the optical loss per cell is approximately 2%, and the loss per polarizer is +6%, the net effect on overall transmission efficiency would be in the range 0% to +2%. In summary, the design appears to increase off-axis contrast, as intended, with a neutral to slightly positive impact on overall optical efficiency.

#### Multispectral analysis software

The package developed at CRI for this work, entitled "PCA Tool" has been brought to completion and provides all core features used for spectral discrimination, including principal component analysis and segmentation, along with data acquisition and display. This package is written for the Windows 95/98 environment in the high-level language Python. Support is included for popular digital cameras including Photometrics, Princeton Instruments, Apogee Instruments, and the Cooke SensiCam. Software development is inherently an ongoing process, in the sense that there is a continual pressure for new features, and a constant need to update to maintain currency with evolving standards such as the upcoming Windows 2000 platform. These factors, along with a desire for cross-platform support (for Linux and/or Mac users) will probably drive CRI to issue a new release of this software package sometime in the next 6-9 months.

#### Repair to imaging spectrometer

During this period, the circuitry that reads out the 2048 element linear photodiode array on the NIR spectrometer failed, apparently due to reasons of static electricity. This system, purchased in 1998, has been categorized as obsolete by the manufacturer (EG&G) and is no longer supported. Since the manufacturer would not repair it, CRI personnel worked to isolate and identify the particular component that had failed, and did so; unfortunately, the component is a custom-programmed gate-array logic (GAL) chip developed by EG&G, for which they could no longer locate the programming file. Thus there was no way to obtain a new chip, nor was there adequate documentation to develop programming to make a replacement GAL chip.

Since EG&G was no longer supporting the 2048 element photodiode array, this meant the NIR spectrometer could no longer be read. After prolonged discussions between CRI and EG&G, the latter firm agreed to supply a 1024 element photodiode array along with the appropriate read-out circuitry, in return for the broken 2048 element array and circuitry. A spare set was also purchased by CRI, in the event this latter system is scheduled for obsolescence as well. Finally, mechanical elements were designed and constructed to utilize the new, smaller array. These eliminated the previously-used 2x optical relay lens arrangement and placed the photodiode array directly at the focal plane of the spectrometer.

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The 1024 element array provides a lower resolution, which is sufficient for characterizing the materials used in filter construction and for assessing out-of-band leakage, but not for

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making measurements of passband shape or peak transmission. This means that the Spex 0.5M conventional swept-grating spectrometer must be used for these measurements. Since the latter constitute only a small number of measurements, performed as acceptance tests after final filter assembly, the impact on work flow is not significant.

#### Applications analysis

Dr. Treado has been demonstrating the utility of Raman chemical imaging with LCTFs, in a range of applications. In addition to work ongoing in a variety of maturing application areas, including semiconductors, pharmaceuticals and polymers, Dr. Treado has been extending LCTF Raman chemical imaging to the analysis of corrosion, airborne particulate matter and fuel cells.

##### a) Corrosion

Application to corrosion monitoring has been demonstrated, including the study of accelerated corrosion in tantalum (Ta) storage vessels exposed to actinide (plutonium and uranium) surrogates, including cerium oxide, under acidic conditions. Raman chemical imaging performed in combination with other microanalytical techniques including scanning electron microscopy (SEM) and infrared microscopy reveals the molecular composition of corrosion byproducts. This information is being used by materials scientists to design next generation storage vessels.

##### b) Airborne particulate matter

Application to the characterization of small airborne particles has been demonstrated. Raman chemical imaging, enabled by LCTF technology, is well suited to the molecular characterization of particles smaller than 2.5  $\mu$ . Particles on this size scale are small enough to be aerodynamic and can be respired. As a result, there are health effects associated with these materials. Understanding the molecular components found in these particles is important to a basic understanding of health effects associated with air quality.

##### c) Fuel cells

Application to mixed oxide (MOX) fuel cells has been demonstrated. MOX fuel cells are mixtures of uranium oxide and plutonium oxide and are a candidate source of commercial nuclear fuel. LCTF Raman chemical imaging has been used to assess the molecular phase of a residual gallium component present at trace levels. Raman chemical imaging is a candidate metrology technique for the routine detection of this trace contaminant in commercial grade fuels.

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# **SBIR PHASE II SEMIANNUAL REPORTING FORMAT**

**SEMIANNUAL REPORTS MUST BE ATTACHED TO A SMALL BUSINESS INNOVATIVE RESEARCH (SBIR) PHASE II REPORT COVER SHEET.**

**Reporting Period:** (From) 3/1/99 (to) 12/30/99

**Total Estimated Expenditures\* this reporting period:** \$ 80,072

**Cumulative Estimated Expenditures\*:** \$ 296,753

<b>Principal Investigator/ Key Personnel (Identify)</b>	<b>Estimated Level of Effort/ Person Months</b>
1. <u>P. Miller</u>	<u>1.7</u>
2. <u>C. Kadamus</u>	<u>1.8</u>
3. _____	_____
4. _____	_____

**Subcontractor(s) Utilized and Services Provided:**

ChemIcon, research assistant support

**Consultant(s) Utilized and Services Provided:**

Dr. Pat Treado, applications analysis consulting

**Identification of Equipment Purchased:**

1. \_\_\_\_\_
2. \_\_\_\_\_

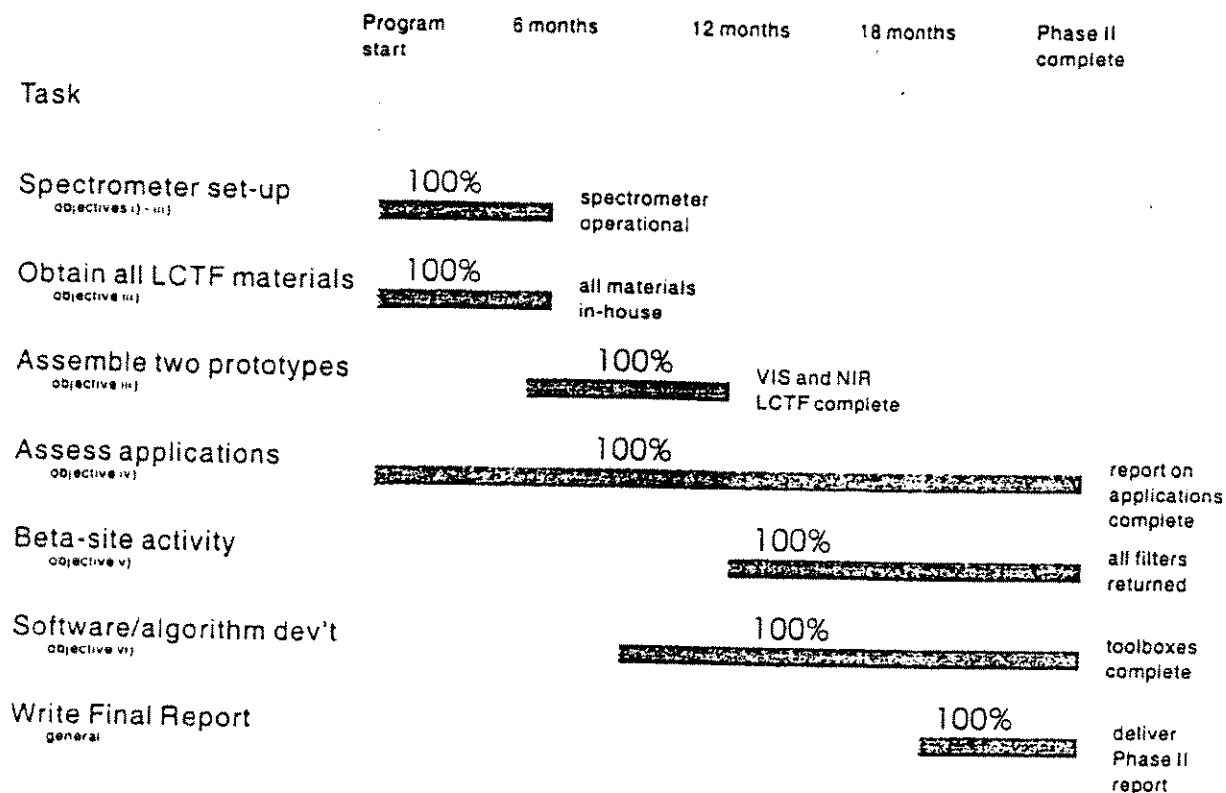
Attach technical report covering accomplishments, milestone progress or completion, and problems encountered this reporting period (report against milestone tasks stated on project milestone chart).

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\*"Estimated Expenditures" means a good faith estimate of actual expenditures for this award.

## Appendix 1. SBIR Phase II Milestone chart



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### Summary of Phase II results

This SBIR had as its goal the commercialization of narrow-band liquid crystal tunable filters (LCTFs) for integration into microscopes for high-definition Raman imaging of samples. All project goals were met successfully, with notes on specific objectives (from the Phase II proposal) as follows:

#### Objective i)

to utilize improved designs to improve the transmission of Raman LCTF filters, resulting in a value at least twice that of the Phase I prototype

The improved design replaced 14 conventional Lyot stages with 7 split-element Evans stages, to achieve the same degree of filtration with twice the optical throughput. Evans stages place more stringent requirements on liquid crystal tuning elements, and on the characterization of the quartz and  $\text{LiNbO}_3$  retarders: since there are a total of three such elements per stage, rather than one, tolerances are proportionally tighter.

The initial Phase II Evans stage barely met the requirement for tuning accuracy, until it was realized that the liquid crystal cells for the outer retarder elements could be built with a smaller tuning range (since two cells and retarders act in concert): by halving the tuning range, one might expect to reduce errors two-fold. Actually, a nearly four-fold reduction was achieved, because use of thinner cells produced correspondingly higher electrical capacitance, leading to improved signal-to-noise in the capacitance-based servo tuning circuitry. This, together with the halved optical tuning range, led to the nearly four-fold improvement overall.

Characterization of the  $\text{LiNbO}_3$  elements to the required accuracy involved construction of a thermally controlled stage. This was built using a controlled water recirculator to define the temperature at two heatsinks, between which the optical retarder was mounted. Windows bonded to the heatsinks permit light to pass through the sample while eliminating convection or other thermal contact with the ambient environment. Scanning is typically done at  $23.0 \pm 0.02^\circ\text{C}$ , to minimize the time needed for parts to reach scan temperature from ambient. Through use of this stage, characterization errors were reduced to the point of insignificance ( $< 1/50 \lambda$ ).

Changing to the Evans design required considerable development of new software algorithms in the embedded microcontroller within the filter electronics. These changes were essential to insure that, in tuning, the outer elements of a given Evans stage undergo order hops from e.g.  $(N+3/4)\lambda$  to  $(N+1/4)\lambda$  in synchrony. New tuning rules were devised to insure that this and other tuning rules were met.

A visible-range filter (500 - 750 nm) was then constructed using the Evans design. It comprises two modules, the first with 4 Evans stages, and the second with 3 Evans stages and 3 Lyot stages. Each optics module thus had 12 liquid crystal cells, and the two modules were controlled by separate electronics modules; the two modules were tuned together connected by a computer via a pair of RS-232 ports. This filter achieved 32% peak transmission at 630 nm, slightly besting the Phase II objective of 30%. The filter

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bandwidth, free spectral range, and image quality were unaffected by the use of the Evans design, as anticipated.

The Evans design is not without its limitations, however. Dr. Treado discovered that the contrast for off-axis rays is somewhat lower than for the previous design. While sufficient for most samples, the filter had inadequate contrast at off-center points when the sample exhibited high levels of background fluorescence. To deal with this, the PI developed a hybrid design for use in Phase III work, which restores essentially all of the lost contrast without a penalty in transmission efficiency. The hybrid design replaced the highest-order two Evans stages with wide-field retarder stages, utilizing achromatic half-wave plates made up of z-compensated laminate films. Further, Mylar is replaced with z-compensated laminate films throughout the design, and a redundant Lyot stage is removed.

Objective ii)

to develop a near-IR version of the Raman LCTF which extends the long-wavelength operating limit from the present value of 700 nm to a minimum of 1050 nm

A near-IR version was designed and constructed using suitable coatings, materials, and construction, exactly as described in the Phase II proposal. It performed successfully, with actual values of bandwidth, free spectral range meeting the design targets. The filter achieved 31% peak transmission at 900 nm.

Objective iii)

to construct and characterize a minimum of one visible and one NIR range Raman LCTF which incorporates these improvements

As noted above in discussion of objectives i) and ii), this was performed and the filters were observed to meet all performance targets.

Objective iv)

to assess experimentally the benefits of Raman LCTF imaging in key areas including semiconductor, biomedical, and pharmaceutical measurements

Dr. Treado has used the LCTFs to assess various chemical systems which benefit from Raman imaging. As per the Plan of Work, the systems selected for study have been drawn from a diverse range of applications. In addition, he has investigated a technique which exploits the continuously-tunable LCTF to resolve energy shifts well below the filter's FWHM, by making very fine adjustments to the center wavelength and performing numerical analyses of the resultant images.

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a) Semiconductors

In the semiconductor field, Dr. Treado has done extensive work on silicon wafers, which indicate that Raman imaging is well-suited to the characterization of silicon systems. Imaging techniques he has demonstrated include both lateral and surface characterization of wafers, using 3-D imaging techniques. Specific application examples include thin-film oxide quantitation, thermal annealing end-point detection, and defect identification

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and review. The results obtained in silicon systems have encouraged him to explore extending this work to other semiconductor systems, including wafers based on III-IV and II-VI materials. These appear especially fruitful, due to the greater complexity of these systems, and the fact that process technology for these materials is less advanced than it is for silicon.

b) Biology and life sciences

In the life sciences, Dr. Treado has begun studying liver diagnostics, particularly the assessment of vitamin A toxicity. This work is still in a preliminary phase, but the first exploratory studies indicate that Raman imaging should permit visualization of vitamin A toxicity on structures in liver tissue.

c) Pharmaceuticals

Pharmaceutical work has centered on the analysis of medicinal tablets. Much of Dr. Treado's effort has been directed towards compositional analysis of such tablets, which is of broad interest to pharmaceutical firms. This can be performed in a non-invasive fashion, either for research purposes or for in-plant off-line Q/A testing. Results to date indicate that Raman imaging can provide a powerful technique for visualizing heterogeneity, such as between active and binder components in tablets.

d) Corrosion

Application to corrosion monitoring has been demonstrated, including the study of accelerated corrosion in tantalum (Ta) storage vessels exposed to actinide (plutonium and uranium) surrogates, including cerium oxide, under acidic conditions. Raman chemical imaging performed in combination with other microanalytical techniques including scanning electron microscopy (SEM) and infrared microscopy reveals the molecular composition of corrosion byproducts. This information is being used by materials scientists to design next generation storage vessels.

e) Airborne particulate matter

Application to the characterization of small airborne particles has been demonstrated. Raman chemical imaging, enabled by LCTF technology, is well suited to the molecular characterization of particles smaller than 2.5  $\mu$ . Particles on this size scale are small enough to be aerodynamic and can be respired. As a result, there are health effects associated with these materials. Understanding the molecular components found in these particles is important to a basic understanding of health effects associated with air quality.

f) Fuel cells

Application to mixed oxide (MOX) fuel cells has been demonstrated. MOX fuel cells are mixtures of uranium oxide and plutonium oxide and are a candidate source of commercial nuclear fuel. LCTF Raman chemical imaging has been used to assess the molecular phase of a residual gallium component present at trace levels. Raman chemical imaging is a candidate metrology technique for the routine detection of this trace contaminant in commercial grade fuels.

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g) Resolution of extremely fine energy shifts

The LCTFs have a resolution (FWHM) of approximately  $8 \text{ cm}^{-1}$ . However, they can be tuned in essentially continuous fashion, by means of the continuously-variable liquid crystal elements. By taking a series of images through the LCTF while it is tuned in fine steps, it should be possible to resolve energy shifts which are considerably below the FWHM. The limit for this type of observation is set by the spatial and spectral non-uniformities of the filter, by thermal drift in the LCTF, and by tuning errors in its spectral scale. The power of this approach may prove to be quite significant, in that a relatively broad LCTF can be employed, compared to the spectral shifts which must be resolved.

Alternative approaches to resolving energy shifts narrower than the instrumental FWHM are more complex than those based on LCTFs. For example, experiment based on spectrometers with fixed detectors such as CCDs, have no ready analogue to this technique and must resort to very high readout densities, or mechanical rocking mechanisms on the grating and/or optics. However, it is straightforward to do so with the LCTF.

Using this technique, Dr. Treado has resolved energy shifts of under  $0.1 \text{ cm}^{-1}$ , or  $1/80^{\text{th}}$  the LCTF bandpass. This level of spectral resolution, coupled with a high-definition spatial image, allows segmentation of features and structures with only the slightest of spectral differences. It is believed that this represents a significant advance in sensitivity for a Raman imaging experiment.

Objective v)

to make at least one of these LCTF instruments available to beta-site researchers for high-definition Raman imaging, on a revolving basis

This objective was accomplished, with two instruments made for use by beta-site researchers during Phase II. This exposure in turn led to at least one commercial order for an LCTF Raman filters, after the beta-site evaluation was concluded. The commercial filter has been built and delivered to the researcher team involved, and is in routine use.

Objective vi)

to develop data analysis methods which exploit the newly-available imaging spectroscopic information, and which render the large data sets tractable

A Windows 95/98 program was developed at CRI for the acquisition and analysis of imaging spectroscopic datasets, using the LCTF. This program, "PCA Tool", is the primary software package used in our laboratory for multispectral image analysis. It contains drivers for most popular digital cameras (Princeton, Photometrics, Cooke, and Apogee brands), and provides for PCA analysis, segmentation, and spectral analysis. Dr. Treado, as part of the present project and his ongoing research, has developed additional techniques for application-specific analyses of particular sample systems as noted above in the summary of application results.

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### **Markets and commercial applications identified in the Phase II work**

The applications developed by Dr. Treado represent clear indications of markets for a Phase III product, to researchers active in these areas. There may also be a market for turnkey instruments that address one or more of these application areas, although the costs of developing such an instrument (and the expertise base involved) place such an effort beyond reach for CRI. Rather, a firm such as ChemIcon would have to play the lead role in developing instruments for e.g. pharmaceutical or semiconductor quality control uses. In this case, CRI would act as a supplier of the enabling technology, the Raman LCTF component.

### **Problems and remaining research objectives**

There are no outstanding unresolved issues that were slated to be addressed in Phase II. Two topics were identified which may be pursued as part of CRI's ongoing work.

As noted above, the Evans design developed in Phase II solved nearly all problems, as hoped. However, its lower off-axis contrast led to a need for a yet-further optimized design when working with highly fluorescent samples. This design has been developed in Phase II and could be produced in Phase III, if there is a demand.

The other topic is to maintain, expand, and improve the PCA Tool software, since this appears to provide a broadly useful capability. It is clear, having developed such a package, that it is of enormous benefit in Raman LCTF imaging and other types of multispectral LCTF imaging. Many supposedly simple systems have been observed to yield a wealth of information when analyzed with these tools, and this area will certainly merit further exploration in the future.

### **Publications**

1. Jon R. Schoonover, Forrest Weesner, George J. Havrilla, Mark Sparrow, and Patrick Treado, **Integration of Elemental and Molecular Imaging to Characterize Heterogeneous Inorganic Materials**, *Appl. Spectrosc.* **52**, (1998) 1505-1514.
2. Hannah R. Morris, Branka Munroe, Rose A. Ryntz, and Patrick J. Treado, **Fluorescence and Raman Chemical Imaging of Thermoplastic Olefin (TPO) Adhesion Promotion**, *Langmuir* **14** (1998) 2426-2434.
3. Christopher T. Zugates and Patrick J. Treado, **Raman Chemical Imaging of Pharmaceutical Tablet Content Uniformity**, *Internet J. Vib. Spect.* ([www.ijvs.com](http://www.ijvs.com)) **2**, 4, section 5, (1998).
4. Michael D. Schaeberle, Hannah R. Morris, John F. Turner II, and Patrick J. Treado, **Raman Chemical Imaging Spectroscopy**, *Anal. Chem.* **71**, (1999) 175A-181A.
5. Hannah R. Morris, John F. Turner II, Branka Munroe, Rose A. Ryntz, and Patrick J. Treado, **Chemical Imaging of Thermoplastic Olefin (TPO) Surface Architecture**, *Langmuir* **13**, (1999) 2961-2972.
6. Jon R. Schoonover, Andrew Saab, Jon S. Bridgewater, George J. Havrilla, Christopher T. Zugates, and Patrick J. Treado, **Raman/SEM Chemical Imaging of a Residual Gallium Phase in a Mixed Oxide Feed Surrogate**, *Inorg. Chem.* (2000) submitted.

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**Commercialization report - DMI-9703950**

This report covers the period from 1 September 1998 through the present.

**Patents**

No inventions have been made during the Phase II project. No patents have been sought by CRI for the technology involved, nor for the use of the Raman LCTF system in particular applications. No licenses to this technology are contemplated.

**Sales**

CRI has sold 3 Raman LCTF systems during this interval, and an order for a fourth is due imminently. These filters have a list price of \$32,000 each, and are incorporated into larger, considerably more expensive (\$200,000) instrumentation systems by our customers.

The technology used to achieve extremely narrow bandpass with high throughput in the Raman LCTFs, has led to a related product line of long-wavelength NIR filters for use over the range 850 -1700 nm. This product has enjoyed sales of approximately \$200,000 in the last year, and demand appears to be growing.

**Spin-offs**

CRI has not created any spin-off divisions or ventures during this interval.

**Changes in company employment levels**

During this reporting interval, CRI employment rose from 20 full-time employees to 28 full-time and 2 part-time (co-op) student positions.

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**COHEN PONTANI LIEBERMAN & PAVANE LLP**

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Marilyn Neiman

Enshan Hong  
Technical Advisor

March 20, 2007

***Filed via ECF***

Judge Rya W. Zobel  
U.S. District Court of Massachusetts  
John Joseph Moakley Courthouse  
1 Courthouse Way  
Boston, MA 02210

Re: Docket No. 05-10367-RWZ  
Miller et al. v. Treado et al.  
Our File No.: 34250-60L

Dear Judge Zobel:

At the pretrial conference on the above-identified litigation scheduled for this Thursday, March 22, 2007, at 3:00 PM in Courtroom 12, counsel for plaintiffs would like to raise the following issues:

**(1) Defendants' Reissue Proceeding**

On January 31, 2007, defendants filed an amendment in their pending proceeding before the Patent Office to reissue U.S. App. Ser. No. 6,734,962 ("the '962 patent-in-suit"), in which they ask the Patent Office to ***completely delete*** Claims 1-6. The inventorship claim currently being litigated in this action is based on Claims 1, 3, and 4 of the '962 patent-in-suit. See, e.g., ¶¶31-32 of the Complaint [D.E. 1]. Defendants' motive is clear: to moot the present action by having the Patent Office reissue the '962 patent-in-suit without Claims 1, 3, and 4. Although the Court denied plaintiffs' previous motion to order defendants to stop their reissue proceeding [D.E. 11], defendants at that time had only slightly amended the claims of the '962 patent-in-suit. Because defendants have now asked the Patent Office to completely delete the basis for this lawsuit from the '962 patent-in-suit, plaintiffs believe it is appropriate for the Court to revisit the topic of defendants' reissue proceeding. If the Court decides it is acceptable, plaintiffs will file a second motion to order defendants to stop their reissue proceeding.

In this regard, it should be noted that defendants have apparently suggested to the Patent Office Examiner, in undocumented telephone interviews, that this Court has stayed all actions on the '962 patent-in-suit, which thereby requires, under Patent Office rules, that the Examiner hasten the examination and reissuance of the patent. At the least, plaintiffs ask that defendants be required to file a statement with the Patent Office, unambiguously informing the Patent Office that there is an inventorship claim concerning Claims 1, 3, and 4 of the '962 patent-in-suit actively being litigated in the District Court of Massachusetts.



Judge Rya Zobel  
 District Court of Massachusetts  
 March 20, 2007  
 Page 2

**(2) Discovery concerning Defendants' Malpractice Lawsuit on the '962 Patent-in-suit**

Plaintiffs have discovered that, before the complaint in the instant action was filed, the law firm that prosecuted the '962 patent-in-suit, Buchanan Ingersoll, had sued defendants in Pennsylvania State Court for unpaid bills totaling \$668,181.33. After the complaint in this action was filed, on May 23, 2005, defendants entered a single counter-claim for malpractice against Buchanan Ingersoll in the Pennsylvania case, on the sole basis that "Buchanan breached [the] duty to exercise reasonable care by drafting and prosecuting patent claims [in the '962 patent-in-suit] that were unnecessarily overbroad in light of the Prior Art" (the "Prior Art" consists of two articles, one of which was written by defendant Treado and plaintiffs Hoyt and Miller, and was the outcome of the collaboration between plaintiffs and defendants which is the factual basis of the present inventorship action).

The focus of the malpractice suit in Pennsylvania is the breadth of the subject matter claimed in the '962 patent-in-suit—there can be no argument that the Pennsylvania lawsuit is not "relevant to the subject matter involved in [this] action". Despite this, defendants have not produced a single document from that lawsuit (not even the publicly-disclosed documents, such as the original complaint), and have told plaintiffs that the "documents regarding [the] legal malpractice action between ChemImage and Buchanan Ingersoll have absolutely nothing to do with Plaintiffs' inventorship claim regarding the '962 Patent." Plaintiffs have complied with LR 37.1 concerning defendants' withholding of all documents from their malpractice lawsuit based on the claims in the '962 patent-in-suit, but it seems the Court might provide a quick answer on this matter at the conference, thereby obviating the need for motion practice.

**(3) Defendants' Noncompliance with the Stipulated Protective Order**

Plaintiffs have also fully complied with LR 37.1 on another issue, which seems too trivial to bring up with the Court, except for the fact that defendants have refused to respond in any way to our communications on the subject.

When the protective order in this case was originally being debated, the parties came up with a compromise to limit the access to material designated "CONFIDENTIAL" to only two people (besides the lawyers, experts, etc.)—two people for the defendants, two people for the plaintiffs:

4. Unless otherwise ordered by the court or permitted in writing by the designating party, a receiving party may disclose Protected Material only to:
  - (a) The receiving party's Outside Counsel ...
  - (b) The receiving party's Experts (as defined and limited in this Order) ...
  - (c) **Two individuals designated by the receiving party** from among the officers, directors, and employees of the receiving party who have signed the "Agreement to be Bound by the Protective Order" (Exhibit A);

Stipulated Protective Order [D.E. 38-2], p. 5, §E.4 (emphasis added)

Plaintiffs duly designated plaintiff Peter Miller as one of the two designated individuals under §E.4(c) of the Stipulated Protective Order, and, when defendants asked plaintiffs to



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provide any Agreements signed by any designated individuals, plaintiffs promptly forwarded Miller's signed Agreement. By contrast, plaintiffs have asked defendants for their signed Agreement(s) four times in the last three months, and defendants have not responded.

If defendants are obeying the Stipulated Protective Order, there are only two choices. One, defendants have a signed Agreement by one or both of the individuals designated under §E.4(c) of the Stipulated Protective Order, but are refusing to produce the signed Agreement(s) to plaintiffs for some unknown reason. Two, no one at ChemImage, including Patrick Treado, has signed the Agreement, as required under the Stipulated Protective Order, and thus no one at ChemImage, including Patrick Treado, has had access to any information designated "CONFIDENTIAL" by plaintiffs in this lawsuit.

Such a trivial matter as producing a signed Agreement should not require the Court's intervention; however, defendants' complete lack of response has made plaintiffs justifiably nervous about who, on defendants' side, has had access to plaintiffs' CONFIDENTIAL information. Plaintiffs seek the Court's assistance in directing defendants to produce the Agreements signed by their designated individuals, thereby obviating the need for motion practice.

**(4) Scope of Discovery**

It is plaintiffs' understanding that discovery has been limited to the inventorship issue in this action. See, e.g., this Court's Order [D.E. 83]; and Feb. 7, 2007 Elec. Order on Plaintiffs' Motion for a Protective Order [D.E. 92] on questions in Peter Miller's deposition. A deposition is scheduled for Friday, March 23, 2007, the day after the Court conference, and plaintiffs would like the Court's assistance in preventing defendants from "going off the reservation", so to speak. As plaintiffs have told defendants, plaintiffs believe that the deponent, Barry Logue, knows nothing substantive about who invented what in the collaboration between plaintiffs and defendants in the 1990's. However, as an ex-salesperson and a present investor with plaintiff CRI, a privately-held company, Mr. Logue may know sensitive business information completely unrelated to the inventorship issue in this case. Based on defendants' in-depth questioning concerning sensitive business information completely unrelated to the inventorship issue in past depositions, plaintiffs ask that the Court confirm the present scope of discovery is limited to the inventorship issue. Mr. Logue, a third party witness, should not have to endure hours of questions about the sensitive business information of plaintiff CRI.

**(5) Defendants' Motion [D.E. 100] to Amend the Scheduling Order**

This pending motion has been completely briefed by the parties.



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Very truly yours,

**COHEN PONTANI LIEBERMAN & PAVANE LLP**

**for Plaintiffs Peter J. Miller, Clifford Hoyt,  
and Cambridge Research & Instrumentation**

/s/ Teodor J. Holmberg  
(BBO#634708)

cc (via ECF): Paul D. Weller, Esq.  
Anthony J. Fitzpatrick, Esq.  
Christopher S. Kroon, Esq.

## DECLARATION

Edward S. Yeung

I. BACKGROUND

## 1. QUALIFICATIONS

I, Edward Szeshing Yeung, received my A.B. in chemistry from Cornell University in 1968 and my Ph.D. in Chemistry from the University of California at Berkeley in 1972. Since then, I have been on the chemistry faculty at Iowa State University, where I am currently Robert Allen Wright Professor and Distinguished Professor in Liberal Arts and Sciences. My research interests span both spectroscopy and chromatography. I have published in areas such as nonlinear spectroscopy, infrared spectroscopy, Raman spectroscopy, laser-based detectors for chromatography, capillary electrophoresis, trace gas monitoring, single-cell and single-molecule analysis, DNA sequencing, and data treatment procedures in chemical measurements. I am an Associate Editor of Analytical Chemistry, the top journal in the field. I served on the editorial advisory board of Progress in Analytical Spectroscopy, Journal of Capillary Electrophoresis, Mikrochimica Acta, Spectrochimica Acta Part A, Journal of Microcolumn Separations, Electrophoresis, Journal of High Resolution Chromatography, Chromatographia and Journal of Biochemical and Biophysical Methods. I was awarded an Alfred P. Sloan Fellowship, was appointed Honorary Professors of Zhengzhou University, Zhongshan University, Xiamen University and Hunan University, and was elected Fellow of the American Association for the Advancement of Science and of the Society for Applied Spectroscopy. I received the ACS Division of Analytical Chemistry Award in Chemical Instrumentation, 4 separate R&D 100 Awards, the Lester W. Strock

1 Award, the Pittsburgh Analytical Chemistry Award, the L. S. Palmer Award, the ACS  
2 Fisher Award in Analytical Chemistry, the Frederick Conference on Capillary  
3 Electrophoresis Award, the Eastern Analytical Symposium Award in Analytical  
4 Chemistry, the ACS Award in Chromatography, the International Prize of the Belgian  
5 Society of Pharmaceutical Sciences, the Eastern Analytical Symposium Award in  
6 Separation Science, the Ralph N. Adams Award in Bioanalytical Chemistry, the Golay  
7 Award, and the Chicago Chromatography Discussion Group Merit Award.

8 I have substantial experience in the development of analytical instrumentation,  
9 including but not restricted to spectroscopy, microscopy, and chemical imaging. The  
10 underlined items above are examples of peer-recognition of my many scientific  
11 contributions in the fields relevant to the present declaration. I have been called by  
12 numerous agencies to evaluate scientific proposals and scientific publications with  
13 respect of merit and novelty in my capacity as editor of journals and as chair or member  
14 of funding panels. In particular, I was a member of the National Academy of Sciences  
15 Committee on Chemical Imaging in 2005 and coauthored the report "VISUALIZING  
16 CHEMISTRY : THE PROGRESS AND PROMISE OF ADVANCED CHEMICAL  
17 IMAGING" published in 2006 by the NATIONAL ACADEMIES PRESS Washington,  
18 D.C. [[www.nap.edu](http://www.nap.edu)]. I have given approximately 700 invited lectures worldwide, many  
19 of which were in the areas of spectroscopy and chemical imaging. I have published  
20 approximately 400 articles in scientific journals dealing with analytical and physical  
21 chemistry. Many of these involve chemical imaging (publications No. 40, 44, 59, 81, 92,  
22 94, 109, 116, 151, 163, 164, 171, 173, 176, 184, 191, 208, 210, 215, 231, 232, 248, 284,  
23 292, 293, 294, 313, 314, 323, 327, 329, 330, 331, 332, 334, 342, 358, 372, 377, 385, 392)

1 and/or microscopy (publications No. 234, 256, 262, 264, 267, 269, 271, 276, 281, 286,  
2 290, 291, 295, 297, 303, 304, 308, 309, 315, 317, 322, 328, 340, 343, 344, 348, 349, 350,  
3 354, 359, 360, 361, 362, 364, 365, 366, 367, 370, 371, 373, 374, 375, 379, 380, 382, 383,  
4 384, 386, 387, 388, 389, 391, 395, 396). I have published in peer-reviewed international  
5 journals on Raman (publications No. 8, 9, 10, 21, 28, 29, 39, 69, 90) and on infrared  
6 (publications No. 11, 12, 13, 16, 17, 18, 23, 27, 45, 70, 111) spectroscopies. In addition, I  
7 hold 22 issued U.S. patents on analytical instrumentation, some of which are in the area  
8 of chemical imaging (U.S. Patents No. 5,192,407, 5,324,401, 5,498,324, 5,582,705,  
9 5,741,411, 6,788,414). I have written, submitted, and have been successful in competing  
10 for numerous scientific proposals to various funding agencies, including SBIR Phase I  
11 and Phase II proposals and a NIST-ATP proposal. I have also served on numerous review  
12 panels on behalf of various funding agencies, including panels that review SBIR Phase I  
13 and Phase II proposals.

14 My curriculum vitae attached here as Schedule A, contains further statements of  
15 my qualifications as an expert in the subject matter of this declaration. In addition, I have  
16 previously served as an expert witness within the last four years in the case of Bio-Rad  
17 Laboratories, Inc. v. Applera Corporation, Case No. C02-5946 JW.

18

## 19 2. PURPOSE AND SCOPE

20 I have been asked by counsel from Morgan, Lewis & Bockius, LLP, Philadelphia,  
21 Pennsylvania, to offer my opinions on the following matters  
22 (a) differences between U.S. Patent No. 6,734,962 ('962 patent)/reissue application No.  
23 11/103,423 and the prior art; and

1 (b) the allegations of co-inventorship raised by plaintiffs in Miller, Hoyt, and Cambridge  
2 Research and Instrumentation, Inc. v. Treado and ChemImage Corp., U.S. District Court  
3 for the District of Massachusetts filed February 24, 2005.

4 In the above capacity, I have been compensated at a rate of \$250.00 per hour.

5

### 6 3. REFERENCE MATERIALS

7 In preparing this report, I have examined the documents listed in the attached  
8 Schedule B. In addition, I have interviewed the people listed in the attached Schedule C.

9 I hereby reserve the right to supplement this report as additional information  
10 becomes available to me.

11

## 12 II. DISCUSSION OF OPINIONS

### 13 1. NEAR INFRARED CHEMICAL IMAGING

14 Imaging refers to the method of obtaining certain location-specific information  
15 from an object. NIR chemical imaging is a specialized subset of imaging that allows one  
16 to identify the chemical composition of an object based on the way the object absorbs  
17 NIR light. These absorption properties of the object are derived from molecular  
18 vibrations and rotations that have well defined energy intervals, thereby creating  
19 spectrally distinct fingerprints at NIR wavelengths. When NIR wavelengths are involved,  
20 these features are generally associated with the vibrational overtones, or multiples of  
21 vibrations, of the molecules. When middle infrared (IR) wavelengths are involved, the  
22 features are generally associated with the fundamental vibrations plus rotations of the

1 molecule(s). When far infrared (FIR) wavelengths are involved, the features are generally  
2 associated with rotations of the molecules.

3 Infrared chemical imaging, regardless of whether the wavelength is at NIR, IR or  
4 FIR, is distinctly different from other types of chemical imaging such as Raman chemical  
5 imaging. The former depends on exciting molecular vibrations and rotations by direct  
6 absorption of light at specific wavelengths while the latter depends on exciting the  
7 molecule to a higher electronic state (discrete or virtual) and relaxing back to an excited  
8 molecular vibrational or rotational state to produce inelastically scattered light. The fact  
9 that these two are completely different spectroscopic techniques is underscored by the  
10 fact that infrared and Raman spectra are mutually exclusive, i.e., vibrational and  
11 rotational features that show up in one mode is typically absent in the other mode.  
12 Furthermore, while infrared intensities are isotropic, Raman intensities are generally  
13 directional and are polarization dependent.

14 There is a form of Raman chemical imaging that involves radiation at NIR  
15 wavelengths. That occurs when a red (e.g. 647-nm Kr ion laser, CRI SBIR Phase I final  
16 report, p. 11, referenced as Document 1-3 p. 14) or NIR (e.g. 1,060 nm Nd:YAG laser)  
17 light source is utilized for Raman excitation. The inelastically scattered Raman radiation  
18 then occurs in the NIR region when energy is transferred to the molecules. The chemical  
19 (molecular) information is different between NIR imaging and Raman imaging. The  
20 radiation detected is different (*vide supra*) regarding directional and polarization  
21 properties. The wavelength requirements of NIR chemical imaging and Raman chemical  
22 imaging in the NIR are different. The former necessarily spans a broad spectral range  
23 (typically 700 nm to 3,300 nm) to access all common vibrational bands while the latter

1 spans only a narrow spectral range immediately to the infrared side of the illuminating  
2 radiation (typically 647-836 nm for 647 nm illumination and 1,060-1,685 nm for 1,060  
3 nm illumination). The methods are also different operationally since the radiation  
4 collected and analyzed is always at the SAME wavelength as the illuminating radiation in  
5 NIR imaging but is always at DIFFERENT wavelengths from the illuminating radiation in  
6 Raman imaging. The system requirements are different since the radiation collected and  
7 analyzed is typically at a SIMILAR intensity range as the illuminating radiation in NIR  
8 imaging but is MUCH WEAKER than the illuminating radiation in Raman imaging. Indeed,  
9 suppression of the illuminating radiation that reaches the detector, e.g. by introducing  
10 additional notch filters, is a major design concern for Raman imaging systems whereas in  
11 NIR imaging it is the illuminating radiation that is specifically detected. It is my opinion  
12 that people skilled in the art of Raman chemical imaging, including those people who are  
13 familiar with Raman chemical imaging in the NIR wavelength region, around the time of  
14 the '962 patent, would not necessarily be knowledgeable in NIR chemical imaging.

15

16 2. U.S. PATENT NO. 6,734,962

17 The '962 patent discloses a near infrared (NIR) chemical imaging system that  
18 consists of 4 components [Claim 1, column 14, lines 20-33]. First, a light source in the  
19 NIR wavelength region illuminates the sample. Second, an optical component collimates  
20 the NIR light that is transmitted, reflected, emitted or scattered from the sample. Third, an  
21 NIR imaging spectrometer selects a range of wavelengths in the beam. Fourth, a detector  
22 collects and records the image that has been filtered. The '962 patent further discloses a  
23 system that combines NIR imagery with visible wavelength imagery [Claim 12, column

1 15, lines 25-39]. Then, a variety of methods to process the collected NIR images are  
2 disclosed [Claims 13-16, column 15, line 41 to column 16, line 48].

3

4 (i) Claims 1 Through 6 in the '962 Patent

5 Claim 1 of the '962 patent [column 14, lines 20-33] consists of 4 components. It  
6 is my opinion that all 4 components as specified are present in the combined system  
7 described in Lewis et al. (U.S. Patent No. 5,377,003). Lewis recites all 4 components in  
8 his Claim 1. Lewis specifically recites "a source of broadband light" and "for use in near-  
9 infrared absorption microscopy", which teaches component (a), followed by "collimation  
10 means for directing said broad-band light", which teaches component (b), followed by  
11 "selecting a near-infrared wavelength of the broadband light to be filtered by the acousto-  
12 optic tunable filter (AOTF) and passed through the acousto-optic tunable filter", which  
13 teaches component (c) since an acousto-optic tunable filter is one kind of near infrared  
14 imaging spectrometer [column 2, lines 49-51], and "a focal plane array detector  
15 comprising a two-dimensional array of charge coupled devices, wherein said charge  
16 coupled devices of said focal plane array detector measure the intensity of light  
17 transmitted or reflected from each of said plurality of spatial locations", which teaches  
18 component (d) since an image comprises detection at a plurality of spatial locations. It is  
19 my opinion that any differences between Claim 1 of the '962 patent and Claim 1 of the  
20 '003 patent would have been obvious to a practitioner of ordinary skill in the relevant  
21 field at that time. Claim 1 of the '962 patent is therefore not patentable over the '003  
22 patent based on the existence of prior art. The dependent claims 2 through 6 in the '962  
23 patent are also not patentable over the '003 patent. These differences would have been

1 obvious because they are nothing more than design choices that would have been within  
2 the skills of persons in the art at that time. I was not able to identify other indicators of  
3 non-obviousness such as a long-felt need for the invention, the failure of others to perfect  
4 the invention, or commercial success.

5

6 (ii) Reissue Application No. 11/103,423

7 I understand that in view of the '003 patent, a reissue application was filed to  
8 amend and to narrow the claims in the '962 patent. Two distinct aspects were included.  
9 First, the word "scattered (light)" was eliminated. This clarifies the confusion between  
10 "elastically scattered light" and "inelastically scattered light." The latter includes Raman  
11 scattering and thus may conflict with Raman chemical imaging in the NIR that is already  
12 known at the time of the filing of the '962 patent. Second, the NIR imaging spectrometer  
13 is specifically defined to be a liquid crystal tunable filter (LCTF). Since the '003 patent  
14 uses an AOTF and not an LCTF imaging spectrometer, conflict with the '003 patent no  
15 longer exists.

16

17 (iii) Claims 1 Through 6 in Reissue Application

18 The examiner of the reissue application (office action dated 9/25/2006) rejected  
19 Claims 1 through 6 of the reissue application, stating that all 4 components in Claim 1  
20 were taught by U.S. Patent No. 5,943,129 in view of U.S. Patent No. 6,711,283. I agree  
21 with the examiner that the '129 patent teaches components (a), (c) and (d) in Claim 1 of  
22 the reissue application and the '283 patent teaches component (b) of the reissue  
23 application. A person skilled in the art would have found the combination of the '129

1 patent and the '283 patent obvious for the reasons stated by the examiner. Claim 1 of the  
2 reissue application is therefore not patentable. Consequently, the dependent claims 2  
3 through 6 in the reissue application are also unpatentable over the '129 patent and the  
4 '283 patent. In addition, the "illumination source" in Claim 2 is taught by the '129 patent  
5 since several illumination sources were specified in the '129 patent, the "infinity-  
6 corrected objective" in Claim 3 is taught by the '129 patent in view of the '283 patent  
7 since the latter specified such an objective, the combination of LCTF and another filter in  
8 Claim 4 is taught by the '129 patent, and the infrared array detectors in Claims 5 and 6  
9 are taught by the '129 patent which specified one type of infrared array detector.

10

11 (iv) Inventions Allowed in the Reissue Application

12 Claim 7 and the associated dependent claims 8 through 11 as well as independent  
13 claims 12 and 13 in the reissue application specify the combination of NIR chemical  
14 imaging with a visible wavelength imagery system. This combination is not found in the  
15 published literature on or before the date of the original patent application. In particular,  
16 this combination is not taught by the '129 patent or by the '283 patent, or is it obvious to  
17 those skilled in the art at the time of the original patent application. I agree with the  
18 examiner that claims 7-13 describe a system that is novel and should therefore be  
19 patentable.

20 The combination of the NIR image with the visible wavelength image offers  
21 valuable information that the individual images cannot provide. Visible wavelength  
22 imagery is the most common form of microscopy. It allows visualization of the  
23 morphology and certain light-blocking properties of the sample. The latter includes

1 absorption, refraction and elastic scattering. The NIR image maps the spatial distributions  
2 of chemical species in the sample based on the fact that NIR absorption wavelengths are  
3 fingerprints of molecular structures. Features in the NIR image must be related to features  
4 in the visible image to facilitate interpretation of the observations in either one. The  
5 recognition of the added value of having both NIR imagery and visible wavelength  
6 imagery is the essence of the inventions disclosed by claims 7-13 of the reissue  
7 application. There is no evidence that any person other than defendant Treado, Matthew  
8 Nelson and Scott Keitzer conceived of the combination of NIR imagery and visible  
9 wavelength imagery in a single platform. On the other hand, there is no documentation  
10 that plaintiffs Miller and Hoyt recognized the salient features of the combination of NIR  
11 imagery and visible wavelength imagery.

12

13 3. COMPLAINT IN MILLER, HOYT, AND CAMBRIDGE RESEARCH AND  
14 INSTRUMENTATION, INC. V. TREADO AND CHEMIMAGE CORP., U.S.  
15 DISTRICT COURT FOR THE DISTRICT OF MASSACHUSETTS FILED  
16 FEBRUARY 24, 2005

17 After the '962 patent was issued, a complaint was filed by Miller, Hoyt and CRI v,  
18 Treado and ChemImage. It alleges, among others, that Miller and Hoyt should be named  
19 co-inventors in the '962 patent. Cited in support of these allegations are:

- 20 (a) the plaintiffs participated in SBIR Phase I and Phase II projects jointly with  
21 the defendants;
- 22 (b) the LCTF filter employed in the system was developed and manufactured by  
23 CRI, including the final version of an Evans split-element LCTF; and

1 (c) plaintiff Hoyt in knowledgeable in the use of infinity-corrected optics in a  
2 Raman imaging microscope.

3 As explained *vide infra*, it is my opinion that each of these, even if true, did not  
4 contribute significantly to the inventions in the '962 patent.

5

6 4. ANALYTICAL INSTRUMENTATION: SYSTEM VS. COMPONENT

7 (i) General Discussion

8 Analytical instrumentation, of which the chemical imaging microscope described  
9 in the '962 patent is one example, consists of many parts and subcomponents. To achieve  
10 its desired function, each of the parts and subcomponents must work in harmony with the  
11 other parts and subcomponents. These parts and subcomponents may be standard  
12 commercially available items or may be one-of-a-kind items that need to be specially  
13 made for the system being assembled. In either case, the parts and subcomponents must  
14 be fitted together in an integrated manner and typically with software to create the  
15 complete system. It is also common that after the initial testing of the system certain parts  
16 or subcomponents have to be substituted, deleted or added to achieve the desired function.  
17 A person may develop one or more of the parts or components of a system without  
18 recognizing the value of the part or component in the integrated system. In such cases,  
19 the person cannot be considered to have contributed significantly to the idea of the  
20 complete system. That is, a person must recognize the value of the combination of each  
21 and every part or component and how each functions in an integrated manner before the  
22 person can make a significant contribution to the development of the system.

1 Explicitly recited in the '962 patent is that "the NIR chemical imaging microscope  
2 combines in a single platform" [column 4, lines 45-56] the four listed parts and  
3 subcomponents of Claim 1 [column 14, lines 22-33]. In addition, the patent states that  
4 "comparing the visible, NIR and NIR chemical images, additional useful information can  
5 be acquired about the chemical composition, structure and concentration" [column 6,  
6 lines 9-12], "the NIR microscope can be used as a volumetric imaging instrument through  
7 the means of moving the sample through focus in the Z, axial dimension" [column 6,  
8 lines 14-16], "depth dependent images can be reconstructed to form volumetric images of  
9 materials without requiring the sample to be moved, again through application of  
10 computational optical sectioning reconstruction algorithms" [column 6, lines 39-43], "a  
11 novel method that is readily employed by the disclosed microscope invention is a method  
12 described as the Chemical Imaging Addition Method" [column 6, lines 52-54], and "this  
13 invention incorporates a comprehensive analysis approach that allows the users to  
14 carefully plan experiments and optimize instrument parameters." [column 10, lines 3-5] It  
15 is my opinion that the chemical imaging system described in the '962 patent provides  
16 additional performance features that are not anticipated by or available through knowing  
17 the characteristics of the individual parts and subcomponents alone. A corollary is that  
18 the assembly of the parts and subcomponents cannot be arbitrary and must involve  
19 judicious optimization to achieve the desired performance of the final system. Parts and  
20 subcomponents that are designed or manufactured for other purposes may need to be re-  
21 optimized when integrated into the final system.

22

23 (ii) Infinity-Corrected Near Infrared Optimized Objective

1 It is well known in the field of microscopy around the time of the '962 patent that  
2 there is a class of lenses called "infinity-corrected objective". Operationally such optics  
3 allows the collected light to be mostly collimated (parallel light rays) over a reasonable  
4 distance in the instrument. The two main reasons for employing such objectives is to  
5 allow placement of intervening optical components that mechanically require the longer  
6 distance and to avoid distortion caused by intervening optical components that have  
7 angular dependent properties. Examples of optical components that have angular  
8 dependent properties include, but are not limited to, certain dielectric filters (bandpass  
9 and bandreject) and notch filters, interferometers (Fabry Perot filters), birefringent  
10 devices, prisms, liquid crystal tunable filters (LCTF), acousto-optic tunable filters  
11 (AOTF), and optical fibers. Even for these optical components, the use of infinity-  
12 corrected objectives is not mandatory but is rather preferred. This is because it is always  
13 possible to produce mostly collimated light from any (positive) objective by adjusting the  
14 working distance (distance between the objective and the object being imaged).

15 The deployment of an infinity-corrected objective, or any other optical component,  
16 in an imaging system requires design and optimization. For a perfectly infinity-corrected  
17 objective, the collected light forms truly parallel rays, but an image cannot be formed at  
18 the detection plane, for example the focal plane array detector. In such a situation, a tube  
19 lens may be introduced to refocus the light rays onto the detection plane. The "summary"  
20 of the '962 patent teaches the use of a NIR optimized microscope with infinity-corrected  
21 objectives to form the image with or without the use of a tube lens. [column 3, lines 50-  
22 53] The "description" of the inventions in the '962 patent teaches the use of infinity-  
23 corrected objectives to form an image without the use of a tube lens [column 5, lines 42-

1 45] "to minimize chromatic aberration, maximize throughput and reduce cost." [column 5,  
2 lines 49-51]. This design resulted from work and discussions at ChemImage between  
3 defendant Treado and Mr. Keitzer. [p. 67-69 of the transcript of the deposition of Scott  
4 Keitzer on November 9, 2006] It is my opinion that an infinity-corrected, or any other,  
5 objective is only relevant to the '962 patent in the context of the complete imaging  
6 system. Without detailed, in-depth understanding of the entire near infrared radiation  
7 chemical imaging system, a person would not be able to incorporate an infinity-corrected  
8 objective into a microscope and achieve the desired function. It is also my opinion that a  
9 person skilled in the art of deploying infinity-corrected objectives in Raman imaging  
10 cannot be assumed to be someone also skilled in the art of deploying infinity-corrected  
11 objectives in NIR imaging.

12 Referring to item 10 (p. 3) of the complaint, it alleges that in 1993 plaintiff Hoyt  
13 conceived of the idea of using infinity-corrected optics in a Raman imaging microscope  
14 and conveyed the idea to defendant Treado. It is my opinion that this item is completely  
15 irrelevant to the '962 patent. First, Raman imaging is different from NIR imaging, as  
16 elucidated *vide supra*. Even if plaintiff Hoyt conceived of the idea of an infinity-corrected  
17 objective during the SBIR Phase I and Phase II work, it was in the context of Raman  
18 imaging and not near infrared chemical imaging. Second, defendant Treado was already  
19 aware of the use of infinity-corrective objectives in a NIR imaging system prior to 1993.  
20 Specifically, on June 9, 1992, when defendant Treado was employed at the National  
21 Institutes of Health, he placed a purchase order for an "infrared microscope objective",  
22 "optimized in the near-infrared", "compatible with an existing laboratory microscope",  
23 and "employed...in our ongoing spectroscopic imaging microscopy studies." [CRI 02913

1 and 02914]. Prior to that, in the research proposal Z01-DK-29001-19-LCP dated on or  
2 before October 1, 1990, the incorporation of "infinity-corrected optics" into a microscope  
3 so that "an increased microscope tube length affords intermediate placement of necessary  
4 optics." [CI 02915 under item 6 of CI 02919]. Also, in another purchase order requested  
5 by defendant Treado and sent to Optical Elements Corporation from the National  
6 Institutes of Health dated March 14, 1991, items 1-LM530T, 1-LM540 and 1-LM550 are  
7 specifically infinity-corrected objectives that are utilized in the microscope system being  
8 purchased. [CI02924]

9 Defendant Treado is already fully knowledgeable in the use of infinity-corrected  
10 objectives (optics) in a NIR imaging microscope prior to any contacts with plaintiff Hoyt  
11 that allegedly occurred in 1993. Furthermore, any alleged conversation with plaintiff  
12 Hoyt had been restricted to the use of infinity-corrected optics in a Raman imaging  
13 microscope, as specified in the complaint. Item 10 in the complaint is thus irrelevant to  
14 the '962 patent.

15 Referring to item 32 of the complaint, the infinity-corrected NIR optimized  
16 microscope objective was stated as a part or subcomponent of the chemical imaging  
17 system as described in the '962 patent. It has already been noted, *vide supra*, that  
18 defendant Treado was someone already skilled in the art of infinity-corrected objectives  
19 as applied to NIR imaging prior to any contacts with CRI and more specifically with  
20 plaintiff Hoyt. Even disregarding that, the part was not designed or manufactured by CRI,  
21 and the implementation of the part in the SBIR Phase I and Phase II project was  
22 exclusively in a Raman chemical imaging microscope that may or may not operate in the  
23 NIR. In connection with the SBIR Phase I and Phase II projects and during any

1 discussions with defendant Treado in connection with such work, I have seen no evidence  
2 that plaintiff Hoyt recognized the potential use of the part in a chemical imaging system  
3 as described in the '962 patent or communicated information related to the ideas leading  
4 to claim 3 of the '962 patent to defendant Treado.

5

6 (iii) Evans Split-Element LCTF

7 The concept behind this version of LCTF originated from a publication authored  
8 by J. W. Evans in 1958 [J. Opt. Soc. Am., Vol. 48, p. 142]. The Evans design is one of  
9 many possible versions of LCTF, some of which were listed in the '962 patent in column  
10 5, lines 34- 41, and column 14, lines 60-67. The list recites Lyot, Evans, Sole,  
11 ferroelectric, Fabry Perot, hybrids of the above, and combinations of one of the above  
12 with other fixed filters. Any of these can serve as the "near infrared imaging  
13 spectrometer" in the chemical imaging system [column 14, lines 29-31]. It is my opinion  
14 that conception of the idea of incorporating any one type of LCTF in a near infrared  
15 chemical imaging system does not imply conception of the idea of the complete infrared  
16 chemical imaging system. In particular, referring to item 11 in the complaint, conception  
17 of the idea of the Evans design, even if true, does not imply that plaintiff Miller made a  
18 significant contribution to the chemical imaging system described in the '962 patent  
19 [column 14, lines 20-21]. Furthermore, since the SBIR Phase I project and the SBIR  
20 Phase II project [items 11, 13 and 18 in the complaint] were directed towards Raman  
21 imaging and since Raman imaging is fundamentally different from NIR imaging  
22 especially in their operational requirements, *vide supra*, any references in these proposals

1 to the deployment of the Evans design are irrelevant to the deployment of the same in a  
2 near infrared radiation chemical imaging system in the '962 patent.

3 Referring to item 31 of the complaint, it is alleged that plaintiff Miller conceived  
4 of using an Evans split-element LCTF in a chemical imaging system using near infrared  
5 radiation. The documents pertaining to the Phase I and Phase II SBIR projects at most  
6 suggest that plaintiff Miller was involved in providing an Evans split-element LCTF that  
7 was later used in Raman imaging in the NIR region. As argued *vide supra*, NIR chemical  
8 imaging as represented in the '962 patent has completely different fundamental  
9 mechanisms and requires completely different operational considerations compared to  
10 Raman imaging in the infrared region. Furthermore, according to item 18 in the  
11 complaint, plaintiff Miller and CRI "built and sold to defendant ChemImage or its  
12 predecessor Evans split-element filters optimized for use in Raman imaging microscopes  
13 using near infrared radiation." Throughout the project periods of the SBIR Phase I and  
14 Phase II projects, the role of CRI with respect to Treado/ChemIcon was as a supplier of a  
15 custom part [purchase order dated 11/12/96, CRI 000186, and another dated 12/10/96,  
16 CRI 000465] that had since become commercially available. That part was originally  
17 designed and developed for a different purpose (Raman imaging in the infrared vs.  
18 infrared chemical imaging) and, being one type of LCTF, it is just one example of an NIR  
19 imaging spectrometer. I have seen no evidence that plaintiff Miller recognized the  
20 potential use of the part in an NIR chemical imaging system or conceived of the idea in  
21 claim 4 of the '962 patent in connection with the Phase I and Phase II SBIR projects.  
22 Finally, on p. 35 of Document 1-4 filed 2/24/2005, under section "patent status", it is  
23 stated that the filters used were covered under separate patents from CRI and that "no

1 patents were filed as a result of the Phase I effort." In the same proposal (p. 31 of the  
2 Phase II proposal and the Phase I final report), the Evans split-element LCTF was  
3 described. Plaintiff Miller also stated the same in his own words [p. 250, line 14 of  
4 deposition dated 10/17/06]. Therefore, even plaintiff Miller himself considered the Evans  
5 split-element LCTF not patentable. Such a conclusion by plaintiff Miller is not surprising  
6 in view of the publication of the specific description of the Evans split-element LCTF in  
7 the Sharp patent (U.S. patent 5,528,393) prior to any documented mention of the Evans  
8 split-element LCTF by plaintiff Miller.

9  
10 5. SBIR PROPOSALS

11 Referring to item 7 in the complaint and subsequent items in the complaint that  
12 refer to Phase I and Phase II SBIR proposals, it is my opinion that being a Principal  
13 Investigator/Project Director does not imply that a person first conceived of the proposed  
14 ideas. Furthermore, performing work in such a funded project does not imply that a  
15 person is involved in any discovery or conception of new ideas that occurs during the  
16 project period. Finally, being named as a coauthor in a scientific publication or having  
17 contributed to the preparation of a report does not infer that a person is involved in any  
18 discovery or conception of new ideas that is stated in the publication or report.

19 In the case of SBIR grants, it is a requirement of those funding agencies that the  
20 Principal Investigator/Project Leader hold less than the equivalent of a half-time position  
21 in an academic institution [e.g., Section 2 (p. 4) of NSF SBIR Solicitation Brochure,  
22 CRI000270]. At the time of submission of the proposals cited in the complaint, defendant  
23 Treado held more than the equivalent of a half-time position at the University of

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1 Pittsburgh [Treado deposition dated October 12, 2006, p. 34, lines 22-25] throughout the  
2 project periods. Therefore, regardless of defendant Treado's contributions to the ideas  
3 and discoveries in those projects, he cannot be designated as the Principal  
4 Investigator/Project Leader. Furthermore, since defendant Treado was a full-time  
5 employee of the University of Pittsburgh, he was precluded from participating in those  
6 projects as a salaried employee of the "company." Defendant Treado's role as  
7 "consultant" on the projects with a limited number of hours was the only type of formal  
8 involvement that would be allowed by his employer, regardless the actual degree of effort  
9 or hours spent by defendant Treado during the project period.

10 It is my experience with SBIR proposals that involve an academic consultant and  
11 a small business, it is typically the former who conceives of the idea, solicits the  
12 cooperation of a small business, and joins the project as a consultant in order to take  
13 advantage of such types of funding and to perform work that is outside the scope of the  
14 regular employment of the former. Often such proposals build on other research projects  
15 that are performed in the laboratory of the former that have potential for  
16 commercialization. In many cases, the latter is incorporated specifically to allow the  
17 former access to such types of funding. An example is the use of a subcontract to the  
18 academic institution to fund work that is performed in the laboratory of the former.

19  
20 **III. GENERAL CONCLUSIONS**

21 Having examined all the documents available to me and having interviewed  
22 several key individuals in the dispute, it is my opinion that the plaintiffs' complaints are  
23 not supported by the facts. At the very heart is the fact that a system contains multiple

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1 components, as in Claims 1 and 7 of the '962 patent. In connection with the Phase I and  
2 Phase II SBIR projects, plaintiff Miller did not conceive of the deployment of the Evans  
3 split-element LCTF filter in view of the '393 patent (Sharp). Even if plaintiff Miller did,  
4 it was in the context of Raman imaging in the near infrared wavelength region and not in  
5 the context of NIR chemical imaging. Further, even if plaintiff Miller conceived of all  
6 possible applications involving the Evans split-element LCFT in connection with the  
7 Phase I and Phase II SBIR projects, it is my opinion that he did not recognize the value or  
8 the technical modifications needed for deploying the same filter in the integrated platform  
9 of a near-infrared chemical imaging system or of a combined near infrared/visible  
10 imagery system. I also have seen no evidence that, in connection with the Phase I and  
11 Phase II SBIR projects, plaintiff Hoyt conceived of the deployment of the infinity-  
12 corrected objective in the chemical imaging system in the '962 patent or communicated  
13 such concepts to defendant Treado. On the contrary, the documents show that defendant  
14 Treado had prior experience in using such objectives. Even if plaintiff Hoyt did, it was in  
15 the context of Raman imaging in the near infrared wavelength region and not in the  
16 context of NIR chemical imaging. Further, even if plaintiff Hoyt conceived of all possible  
17 applications involving the infinity-corrected objective, I have seen no evidence that in  
18 connection with the Phase I and Phase II SBIR projects, he recognized the value or the  
19 technical modifications needed for deploying the same objective in the integrated  
20 platform of a near-infrared chemical imaging system or of a combined near  
21 infrared/visible imagery system.

22 As for the '962 patent, I agree with the examiner that prior art exists for Claims 1  
23 through 6, making them obvious over prior art. In contrast, Claims 7-13 of the reissue

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1 application contains all 4 elements of Claim 1 in the '962 patent plus a visible imagery  
2 component. Such a combination is highly valuable but is not anticipated or taught in prior  
3 art. Therefore, it is my opinion that claims 7-13 in the reissue application are novel and  
4 non-obvious.

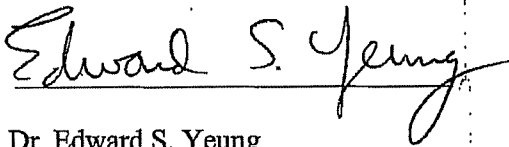
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6

7 Respectfully submitted,

8

9



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11 Distinguished Professor of Liberal Arts and Sciences  
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16

17

18

19 Dated: April 30, 2007

**SCHEDULE A**

**PROFESSIONAL BIOGRAPHY**

**EDWARD S. YEUNG**

**PERSONAL**

Name:	Edward Szeshing Yeung
Date of Birth:	February 17, 1948
Place of Birth:	Hong Kong, B.C.C.
Marital Status:	Married - Anna (Seto) Yeung
Citizenship:	U.S.

**EDUCATION**

High School:	St. Paul's Co-Ed, Hong Kong - 1965
College:	A.B., 1968 - Cornell University, Ithaca, NY, magna cum laude (1965-1968) Ph.D., 1972 - University of California at Berkeley (1968-1972) Thesis: Photochemistry of Single Vibronic Levels of Formaldehyde Research Advisor: Prof. C. Bradley Moore

**EXPERIENCE**

1972-1974	Instructor in Chemistry at Iowa State University and Assistant Chemist in the Ames Laboratory - AEC
1974-1977	Assistant Professor in Chemistry, Iowa State University and Associate Chemist in the Ames Laboratory - USAEC
1977-1981	Associate Professor in Chemistry, Iowa State University and Chemist in the Ames Laboratory - USDOE
1981-1989	Professor in Chemistry, Iowa State University and Senior Chemist in the Ames Laboratory - USDOE
1989-	Distinguished Professor in Liberal Arts and Sciences, Iowa State University, and Senior Chemist in the Ames Laboratory - USDOE
2003-	Robert Allen Wright Chair Professor, Iowa State University

## HONORS AND AWARDS

Phi Eta Sigma

Sigma Xi

U.C. Berkeley Science Fellowship (1970-71)

U.C. Berkeley Chancellor Science Fellowship (1971-72)

Alfred P. Sloan Research Fellow (1974-76)

Honorary Professor, Zhengzhou University, P. R. China (1983)

Arthur D. Little Lecturer, Northeastern University (1987)

ACS Division of Analytical Chemistry Chemical Instrumentation Award (1987)

Mid-America State Universities Association Honor Lecturer (1987-88)

External Examiner, Chinese University of Hong Kong (1988-91)

Fellow, Japan Society for the Promotion of Science (1989)

Federal Laboratory Consortium Award for Excellence in Technology Transfer (1989)

1989 R&D 100 Award (most significant new technical product in 1988)

Honor Lectureship, National Science Council, Republic of China (1990)

Merck Academic Development Fellowship (1990-92)

Lester W. Strock Award, Society of Applied Spectroscopy (1990)

McElvain Seminar, University of Wisconsin (1991)

1991 R&D 100 Award (most significant new technical product in 1990)

Varian Lecturer (First), Centre for Analytical/Environmental Chemistry, Carleton University (1992)

Fellow, American Association for the Advancement of Science (1992)

Federal Laboratory Consortium Award for Excellence in Technology Transfer (1993)

Pittsburgh Analytical Chemistry Award (1993)

Elving Lecturer, University of Michigan (1993)

ACS Fisher Award in Analytical Chemistry (1994)

Centennial Lecturer, University of Texas, Austin (1994)

Dow Distinguished Lecturer, Indiana University (1994)

Research Frontiers Lecturer, University of Iowa (1994)

L. S. Palmer Award, Minnesota Chromatography Forum (1994)

Hach Lecturer, University of Wyoming (1994)

Phi Lambda Upsilon Lecturer, Purdue University (1994)

Distinguished Achievement Award, Chinese-American Chemical Society (1995)

Abbott Lecturer, University of North Dakota (1995)

Honorary Professor, Zhongshan University, P. R. China (1995)

Merck, Frosst, Sharp & Dohme Lecturer, University of British Columbia (1996)

Moses Gomberg Lecturer, University of Michigan (1996)

Frontiers in Chemical Research Lecturer, Texas A&M University (1996)

Henry Werner Lecturer, University of Kansas (1996)

Phi Lambda Upsilon Lecturer, Duke University (1997)

Raymond M. Castle Lecturer, Brigham Young University (1997)

Gary W. Griffin Lecturer, University of New Orleans (1997)

1997 R&D 100 Award (most significant new technical product in 1996)

Frederick Conference on Capillary Electrophoresis Award (1997)

Bayer Lecturer, University of New Hampshire (1998)

Eastern Analytical Symposium Award in Analytical Chemistry (1998)

Haines Lecturer, University of South Dakota (1999)

Honorary Professor, Xiamen University, P. R. China (1999)

Francis Clifford Phillips Lecturer, University of Pittsburgh (2000)

Conover Lecturer, Vanderbilt University (2000)  
 Kolthoff Lecturer, University of Minnesota (2001)  
 J. Clarence Karcher Lecturer, University of Oklahoma (2001)  
 2001 R&D 100 Award (Editor's Choice, most significant new technical product in 2000)  
 ACS Award in Chromatography (2002)  
 International Prize of the Belgian Society of Pharmaceutical Sciences (2002)  
 Honorary Professor (First ever), Hunan University, P. R. China (2002)  
 Burroughs Wellcome Distinguished Lecturer, East Carolina University (2003)  
 Eastern Analytical Symposium Award in Separation Science (2003)  
 Woodward Lecturer, Harvard University (2004)  
 Iowa Inventor of the Year (2004)  
 Ralph N. Adams Award in Bioanalytical Chemistry, inaugural (2005)  
 Habermann Lecturer, Marquette University (2006)  
 M.J.E. Golay Award (2006)  
 Merit Award, Chicago Chromatography Discussion Group (2006)  
 Chang Jiang Scholar, PRC (2007)  
 Fellow, Society for Applied Spectroscopy (2007)

#### CONFERENCE SYMPOSIA ORGANIZED

(\*Denotes current activity)

Chairman, Electronic Spectra Session, XXIX Symposium on Molecular Structure and Spectroscopy, Columbus, Ohio, June 10-14, 1974  
 Chairman to organize Symposium on "Laser-Based Spectroscopic Detectors for HPLC", Fall 1981 ACS Meeting, New York  
 Chairman to organize Symposium on "Laser-Based Ultrasensitive Spectroscopy and Detection", 1983 SPIE Meeting, San Diego  
 Chairman to organize Symposium on "Laser Applications in Analytical Chemistry", Seventh International Conference on Lasers and Applications, San Francisco, November 1984  
 Program Chairman of 1988 ACS Summer Symposium in Analytical Chemistry  
 Chairman to organize Symposium on "Detectors for HPLC and SFC", 1987 Pittsburgh Conference and Exposition, Atlantic City  
 Chairman to organize Symposium on "Detectors in Liquid Chromatography", 1987 Spring ACS Meeting, Denver  
 Chairman to organize Symposium on "Laser Applications in Chemical Analysis", Third International Laser Science Conference, Atlantic City, 1987  
 Chairman to organize symposium on "Laser-based Measurements in Chemical Analysis", 27th Eastern Analytical Symposium, New York, 1988  
 Chairman to organize symposium on "Whither Spectrochemical Analysis", Fall National ACS Meeting, Los Angeles, September, 1988  
 Chairman-Elect, 1989, and Chairman, 1990, Gordon Research Conference in Analytical Chemistry  
 Chairman to organize symposium on "Analytical Spectroscopy", Sixth International Laser Science Conference, Minneapolis, 1990  
 Chairman to organize symposium on "Detectors in Chromatography", 29th Eastern Analytical Symposium, Somerset, NJ, 1990  
 Member, Technical Program Committee for the OSA Topical Meeting on Laser Applications to Chemical Analysis, Salt Lake City, UT, 1992  
 Member, Scientific Committee for the NCI Frederick Conference on Capillary Electrophoresis, 1990-2004

Member, Scientific Committee, 1992 International Symposium on Column Liquid Chromatography, Baltimore, MD  
 Chairman, HPLC-2000 International Symposium on Column Liquid Chromatography, Seattle, WA  
 \*Member, Permanent Scientific Committee, International Symposium on High Performance Capillary Electrophoresis, 1993-present  
 Chairman to organize symposium on "Capillary Electrophoresis", 1994 PharmAnalysis Conference, Atlantic City, NJ, 1994  
 Chairman to organize symposium on "DNA Probes and Sequencing", 1994 FACSS Conference, St. Louis, MO, 1994  
 Member, Scientific Committee, 1994 International Symposium on Column Liquid Chromatography, Minneapolis, MN  
 Member, Scientific Committee, 1996 International Symposium for Liquid Phase Separations, San Francisco, CA  
 Member, Scientific Committee, 1996 Asian Pacific Conference on Capillary Electrophoresis, Singapore  
 Member, Advisory Committee, Conference for Worldwide Chinese Young Scientists, 1997, 2000  
 Member, Program Committee, BIOS '97, 1997  
 Member, Program Committee for Optical Society of America Spring Topical Meeting, 1998  
 Chairman, HPCE '99 International Conference on Capillary Electrophoresis, Palm Springs, 1999  
 Member, Scientific Committee, 1998 International Symposium for Liquid Phase Separations, St. Louis, MO  
 \*Member, Permanent Scientific Committee, International Symposium for Liquid Phase Separations, 1998-present  
 Honorary Advisory Member, Second Worldwide Chinese Symposium on Applied Chemistry, Changchun, P. R. China, 1998  
 Member, Scientific Committee, II Asia Pacific International Symposium on Capillary Electrophoresis, Dalian, P. R. China, 1998  
 Vice Chairman, International Advisory Committee, Third International Symposium of Worldwide Chinese Scholars on Analytical Chemistry, Hong Kong, 1998  
 Member, Scientific Committee, III Asia Pacific International Symposium on Capillary Electrophoresis, Hong Kong, 2000  
 Conference Co-chair, SPIE BIOS 2000 Symposium, San Jose, CA  
 Member, Scientific Committee, IV Asia Pacific International Symposium on Capillary Electrophoresis, Shanghai, 2002  
 Member, International Scientific Committee, Asianalysis V, 2004  
 Member, International Scientific Committee, Asianalysis VI, 2005

#### NATIONAL AND INTERNATIONAL SERVICES

(\*Denotes current activity)

Secretary and Treasurer for Ames Section ACS, 1976; Chair-Elect, 1977; Chair, 1978  
 External Reviewer, Pacific Northwest Laboratory, Analytical Division, Richland, Washington, February 1984  
 Editor, monograph on "Detectors in Liquid Chromatography", Chemical Analysis Series, 1986  
 Editor, Progress in Analytical Spectroscopy, 1985-1988  
 Member of Editorial Advisory Board of Spectrochimica Acta, 1985-1989  
 Member, NIH Metallobiochemistry Study Section, 1986-1990  
 Member, NIH Special Study Section for Small Business Innovation Research, 1986

Member of Editorial Advisory Board of Analytical Chemistry, 1987  
Member of Editorial Advisory Board of Mikrokimica Acta, 1987-1993  
Canvassing Committee of an ACS Award, 1986-1989  
Member of Jury of an ACS Award, 1986-1988, 1999-2001  
Member, Committee on Recommendations for U.S. Army Basic Scientific Research, National Research Council, 1987-1990  
Member, Commission V-4 (Spectroscopy), International Union of Pure and Applied Chemistry, 1987-1995  
External Examiner, Chinese University of Hong Kong, 1988-1991  
Member, Panel to review the human genome projects for the U.S. Department of Energy, 1988-1991, 1993, 1994  
\*Associate Editor in charge of the area of spectroscopy, Analytical Chemistry, 1988-present  
External Reviewer, Lawrence Berkeley Laboratories Instrumentation Program, 1988  
External Reviewer, Oak Ridge National Laboratories Analytical Chemistry Program, 1988  
Member, NIH Special Study Section for Shared Instrumentation Grant, 1988  
Chairman, NIH Metallobiochemistry Study Section for Academic Research Enhancement Awards, 1988  
Member of Editorial Advisory Board of Progress in Analytical Spectroscopy, 1989  
Member, NSF Review Panel for Chemistry Postdoctoral Fellowships, 1989  
Member, NIH Special Review Committee for Technology Development for Genomic Analysis, 1989  
Member, NIH Review Committee for Laser Microbeam Biotechnology Resource, 1989  
Councilor (Elected), American Chemical Society, representing the Division of Analytical Chemistry, 1989-1992  
Member, NIH Special Review Committee for Human Genome Initiative, 1989  
Committee Associate, ACS Joint Board-Council Committee on Science, 1990-1992  
Member, Advisory Panel, Analytical Chemistry Division of Oak Ridge National Laboratory, 1990-1993  
Member, National Academy of Science Panel on New Measurement Technologies for the Ocean, 1990-1992  
Member of Editorial Advisory Board of Spectrochimica Acta Reviews, 1990-1993  
Member, NIH Special Study Section for Biomedical Research Technology Program, 1990  
Member, Ad hoc NIH Metallobiochemistry Study Section, 1991, 1992, 1994, 1995  
Member, Jury for E. O. Lawrence Memorial Award, 1991  
Member, ACS Joint Board-Council Committee on Science, 1993-1995, 1996-1998, 1999-2001  
Member, NSF Review Panel for Small Business Innovation Research, 1993  
Member, Council of the Gordon Research Conferences, 1994-1996  
Chairman, ACS Division of Analytical Chemistry, 1995-1996  
Member, Editorial Advisory Board of Journal of Capillary Electrophoresis, 1994-present  
Member, Editorial Advisory Board of Journal of High Resolution Chromatography, 1994-2001  
Member, NIH Panel to Review Laser Microbeam Resource, 1994  
Member, DOE Panel on Laser Instrumentation, 1995  
Member, Editorial Advisory Board of Journal of Microcolumn Separations, 1996-2000  
Member, DOE Human Genome Site Review Team, 1996, 1997  
Member, Ad hoc Study Section for NIH Research Resources, 1996  
Member, NIH ad hoc Reviewer Panel, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003  
Member, Review Panel for Swedish Research in Analytical Chemistry, 1997  
Member, NSF Review Panel for Small Business Innovation Research, 1997, 1998  
Member, Review Panel for Separation Sciences in Japan, 1997

- \*Member, Advisory Committee of the Institute of Chemistry, Academia Sinica, Taiwan, 1997-present
- Member, External Review Committee, National Taiwan University, Taipei, Taiwan, 1998, Chair, 2004
- \*Member, Editorial Advisory Board of Electrophoresis, 1998-present
- \*Member, Science Advisory Committee, Hong Kong University of Science and Technology, 1999-present
- \*Member, Editorial Advisory Board of Chromatographia, 1998-present
- Member, Editorial Advisory Board of the Journal of Biochemical and Biophysical Methods, 1999-2003
- Member, National Research Council Board on Assessment of NIST Programs, 1999-2001
- External Advisor, University of Hong Kong, 2000-2002
- Member, Committee of Visitors, National Science Foundation, 2001
- \*Member, Advisory Committee for the Institute of Atomic and Molecular Science, Academia Sinica, Taiwan, 2001-present
- \*Member, Physical Sciences Panel, Research Grants Council, Hong Kong, 2001-2003, Chair, 2003-present
- \*Member, International Editorial Board of the Chinese Journal of Chromatography, 2002-present
- \*Member, Advisory Board of the Research Center for Micro-Proteomics Science and Technology, Taiwan, 2002-present
- Member, NSF Review Panel for CAREER Awards, 2003
- Member, National Academy of Sciences Committee on Chemical Imaging, 2005
- \*Co-Editor, Annual Reviews of Analytical Chemistry, 2006-present
- \*Member, External Review Committee, National Tsing Hua University, Hsinchu, Taiwan, 2007

# U.S. PATENTS

E. S. Yeung

1. E. S. Yeung and C. B. Moore, "Isotopic Separation by Photopredissociation"—U.S. Patent #3,983,020 (1976).  
(Patent rights also issued include Canadian Letters Patent No. 1,016,897, French Letters Patent No. 74.02436, Israeli Letters Patent No. 43900, and British Letters Patent No. 1,457,952).
2. E. S. Yeung and S. D. Woodruff, "Refractive Index and Absorption Detector for Liquid Chromatography Based on Fabry-Perot Interferometry"—U.S. Patent #4,455,089 (1984).
3. E. S. Yeung, L. E. Steenhoek, S. D. Woodruff and J. C. Kuo, "Micropolarimeter for High Performance Liquid Chromatography"—U.S. Patent #4,498,774 (1985).
4. S. R. Spurlin and E. S. Yeung, "Sulfide Chemiluminescence Detection"—U.S. Patent #4,555,491 (1985).
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6. S. R. Spurlin and E. S. Yeung, "Apparatus for Use in Sulfide Chemiluminescence Detection"—U.S. Patent #4,634,574 (1987).
7. R. E. Synovec and E. S. Yeung, "Method for Improving the Limit of Detection in a Data Signal"—U.S. Patent #4,875,169 (1989).
8. E. S. Yeung and G. Chen, "Method and Means for a Spatial and Temporal Probe for Laser-generated Plumes based on Density Gradients"—U.S. Patent #4,921,348 (1990).
9. E. S. Yeung and S. L. Chen, "Linearization of Scan Velocity of Resonant Vibrating-Mirror Beam Deflectors"—U.S. Patent #4,984,857 (1991).
10. E. S. Yeung and W. G. Kuhr, "Means and Method for Capillary Zone Electrophoresis with Laser-induced Indirect Fluorescence Detection"—U.S. Patent #5,006,210 (1991).
11. E. S. Yeung, L. B. Koutny, B. L. Hogan, K. C. Chan and Y. Ma, "Means and Method of Detection in Chemical Separation Procedures"—U.S. Patent #5,192,407 (1993).
12. E. S. Yeung and J. A. Taylor, "Multiplexed Fluorescence Detector System for Capillary Electrophoresis"—U.S. Patent #5,324,401 (1994).
13. E. S. Yeung and J. A. Taylor, "Multiplexed Fluorescence Detector System for Capillary Electrophoresis"—U.S. Patent #5,498,324 (1996).
14. E. S. Yeung and Y. Xue, "Noise Suppressing Capillary Separation System"—U.S. Patent #5,540,825 (1996).
15. E. S. Yeung, H-T. Chang, E. N. Fung, Q. Li and X. Lu, "Multiplexed Capillary Electrophoresis System"—U.S. Patent #5,582,705 (1996).

16. E. S. Yeung, H-T. Chang and E. N. Fung, "Capillaries for Use in a Multiplexed Capillary Electrophoresis System"—U.S. Patent #5,695,626 (1997).
17. E. S. Yeung, Q. Li and X. Lu, "Multiplexed Capillary Electrophoresis System"—U.S. Patent #5,741,411 (1998).
18. E. S. Yeung, L. B. Koutny, B. L. Hogan, K. C. Chan and Y. Ma, "Means and Method of Detection in Chemical Separation Procedures"—U.S. Patent #5,879,528 (1999).
19. E. S. Yeung and Y-C. Chang, "Laser Vaporization/Ionization Interface for Coupling Microscale Separation Techniques with Mass Spectrometry"—U.S. Patent #5,917,185 (1999).
20. E. S. Yeung and H. Tan, "Integrated Multiplexed Capillary Electrophoresis System"—U.S. Patent #6,387,234 (2002).
21. E. S. Yeung and X. Gong, "Method of Analyzing Multiple Samples Simultaneously by Detecting Absorption and Systems for Use in Such a Method"—U.S. Patent #6,788,414 (2004).
22. E. S. Yeung and W. Wei, "Size Separation of Analytes using Monomeric Surfactants"—U.S. Patent #6,878,254 (2005).

## BOOK REVIEWS

E. S. Yeung

1. E. S. Yeung, "Laser Light Scattering", an invited Book Review of the monograph by B. Chu, *J. Chem. Ed.* 52, A486 (1975).
2. E. S. Yeung, "The Dynamics of Spectroscopic Transitions", an invited Book Review of the monograph by J. D. Macomber, *J. Am. Chem. Soc.* 98, 6766 (1976).
3. E. S. Yeung, "Liquid Chromatography Detectors", an invited Book Review of the monograph by R. P. W. Scott, 2nd Ed., *LC-GC* 5(11), 994 (1987).
4. E. S. Yeung, "Laser Remote Chemical Analysis", an invited Book Review of the monograph by R. M. Measures, *Appl. Spectrosc.* 42(6), 20A (1988).
5. E. S. Yeung, "Laser Microanalysis", an invited Book Review of the monograph by L. Moenke-Blankenburg, *Appl. Spectrosc.* 44(1), 18A (1990).
6. E. S. Yeung, "Polarized Light in Optics and Spectroscopy", an invited Book Review of the monograph by D. S. Kliger, J. W. Lewis, and C. E. Randall, *Spectrosc.* 7(5), 50 (1992).
7. E. S. Yeung, "A Practical Guide to HPLC Detection", an invited Book Review of the monograph by D. Parriott, *J. Chromatogr.* 641, 203 (1993).
8. E. S. Yeung, "Advances in Near-Infrared Measurements" an invited Book Review of the monograph by G. Patonay, *J. Am. Chem. Soc.* 116, 9810 (1994).

## TECHNICAL REPORTS

E. S. Yeung

1. G. D. T. Tejwani and E. S. Yeung, "Calculated Pressure-Broadened Linewidths of Ozone", IS-3575 Technical Report (1975).

This report summarizes the results in publication #11. This has already found use by air pollution researchers and atmospheric researchers.

2. G. D. T. Tejwani and E. S. Yeung, "Calculated Pressure-Broadened Linewidths of NO<sub>2</sub>", IS-3621 Technical Report (1975).

This report summarizes the results in publication #12. This has already found use by air pollution researchers and atmospheric researchers.

3. G. D. T. Tejwani and E. S. Yeung, "Calculated Pressure-Broadened Linewidths of Hydrogen Sulfide", IS-3904 Technical Report (1976).

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**SCHEDULE B**

DOCUMENTS EXAMINED FOR PREPARATION OF DECLARATION

1. U.S. Patent No. 6,734,962 and associated filing history
2. U.S. Patent No. 5,377,003
3. U.S. Patent No. 5,943,129
4. U.S. Patent No. 6,711,283
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15. Deposition of Matthew Nelson dated 11/8/2006
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**SCHEDULE C**

PERSONS INTERVIEWED FOR PREPARATION OF DECLARATION

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